

2D-NMR

Correlation spectroscopy (COSY) is one of several types of two-dimensional nuclear magnetic resonance (NMR) spectroscopy. Other types of two-dimensional NMR include **J-spectroscopy**, **exchange spectroscopy** (EXSY), and Nuclear Overhauser effect spectroscopy (NOESY). Two-dimensional NMR spectra provide more information about a molecule than one-dimensional NMR spectra and are especially useful in determining the structure of a molecule, particularly for molecules that are too complicated to work with using one-dimensional NMR. The first two-dimensional experiment, **COSY**, was proposed by Jean Jeener, a professor at the Université Libre de Bruxelles, in 1971. This experiment was later implemented by Walter P. Aue, Enrico Bartholdi and Richard R. Ernst, who published their work in 1976.

Principles

A two-dimensional NMR experiment involves a series of one-dimensional experiments. Each experiment consists of a sequence of radio frequency pulses with delay periods in between them. It is the timing, frequencies, and intensities of these pulses that distinguish different NMR experiments from one another. During some of the delays, the nuclear spins are allowed to freely precess (rotate) for a determined length of time known as the **evolution time**. The frequencies of the nuclei are detected after the final pulse. By incrementing the evolution time in successive experiments, a two-dimensional data set is generated from a series of one-dimensional experiments.

An example of a two-dimension NMR experiment is the homonuclear correlation spectroscopy (COSY) sequence, which consists of a pulse (p1) followed by an evolution time (t1) followed by a second pulse (p2) followed by a measurement time (t2). A computer is used to compile the spectra as a function of the evolution time (t1). Finally, the Fourier transform is used to convert the time-dependent signals into a two-dimensional spectrum.

The two-dimensional spectrum that results from the COSY experiment shows the frequencies for a single isotope (usually hydrogen, ^1H) along both axes. (Techniques have also been devised for generating heteronuclear correlation spectra, in which the two axes correspond to different isotopes, such as ^{13}C and ^1H .) The intensities of the peaks in the spectrum can be represented using a third dimension. More commonly, intensity is indicated using contours or different colors. The spectrum is interpreted starting from the diagonal, which consists of a series of peaks. The peaks that appear off of the diagonal are called cross-peaks. The cross-peaks are symmetrical (both above and below) along the diagonal and indicate which hydrogen atoms are spin-spin coupled to each other. One can determine which atoms are connected to one another by only a few chemical bonds by matching the center of a cross-peak with the center of each of two corresponding diagonal peaks. The peaks on the diagonal when matched with cross-peaks are coupled to each other.

For example: a $\text{CH}_3\text{CH}_2\text{COCH}_3$ molecule 2-butanone would show three peaks on the diagonal, due to the three distinct hydrogen groups. By drawing a line straight down from a cross-peak to the point on the diagonal directly above or below it, and then drawing a line from the cross-peak directly across to another peak on the diagonal, one can determine which peaks are coupled. This is done in such a way that the lines from the cross-peak form a 90° angle between the two peaks on the diagonal. The matching peaks, as determined by using the cross-peaks, indicate which hydrogens are coupled, giving a clearer understanding of the structure of the molecule under examination.

To the right is an example of a COSY NMR spectrum of progesterone in DMSO-d₆. The spectrum that appears along both the *x*- and *y*-axes is a regular one dimensional ¹H NMR spectrum. The COSY is read along the diagonal - where the bulk of the peaks appear. Cross-peaks appear symmetrically above and below the diagonal.

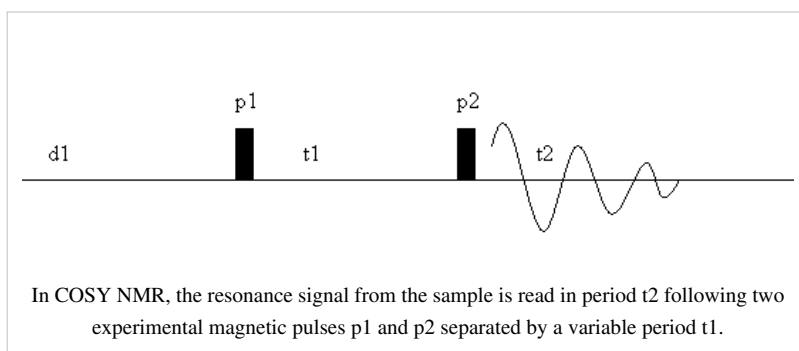
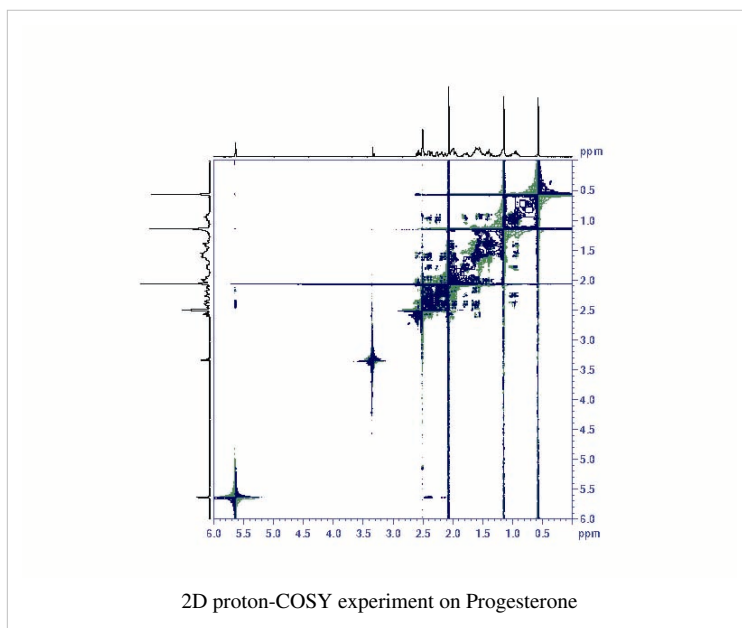
COSY NMR

COSY-90 is the most common COSY experiment. In COSY-90, the sample is irradiated with a radio frequency pulse, p1, which tilts the nuclear spin by 90°. After p1, the sample is allowed to freely precess during an evolution period (t1). A second 90° pulse, p2, is then applied, after which the experimental data are acquired. This is done repeatedly using a series of different evolution periods (t1). At the conclusion of data acquisition the data is Fourier transformed in each dimension to generate the two dimensional spectrum. It is only because the evolution period is varied that cross-peaks appear in the spectrum.

Cross-peaks result from a phenomenon called magnetization transfer. In COSY, magnetization transfer occurs through the chemical bonds rather than through space.

Another member of the COSY family is **COSY-45**. In COSY-45 a 45° pulse is used instead of a 90° pulse for the first pulse, p1. The advantage of a COSY-45 is that the diagonal-peaks are less pronounced, making it simpler to match cross-peaks near the diagonal in a large molecule. Additionally, the relative signs of the coupling constants can be elucidated from a COSY-45 spectrum. This is not possible using COSY-90.^{COSY45_vs_COSY90} Overall, the COSY-45 offers a cleaner spectrum while the COSY-90 is more sensitive. Related COSY techniques include double quantum filtered COSY and multiple quantum filtered COSY.

COSY NMR has useful applications. Organic chemists often use COSY to elucidate structural data on molecules that are not satisfactorily represented in a one-dimensional NMR spectrum. Using cross-peaks, along with the diagonal spectrum, one can often discover much about the structure of an unknown molecule.



NOESY

In NOESY, the Nuclear Overhauser effect (NOE) between nuclear spins is used to establish the correlations. Hence the cross-peaks in the resulting two-dimensional spectrum connect resonances from spins that are spatially close. NOESY spectra from large biomolecules can often be assigned using Sequential Walking.

The NOESY experiment can also be performed in a one-dimensional fashion by pre-selecting individual resonances. The spectra are read with the pre-selected nuclei giving a large, negative signal while neighboring nuclei are identified by weaker, positive signals. This only reveals which peaks have measurable NOEs to the resonance of interest but obviously takes much less time than the full 2D experiment. In addition, if a pre-selected nucleus changes environment within the time scale of the experiment, multiple negative signals may be observed. This offers exchange information similar to EXSY (i.e. exchange spectroscopy) NMR spectroscopy.

HMBC & HMQC

HMQC (Heteronuclear Multiple Quantum Coherence) and HMBC (Heteronuclear Multiple Bond Coherence) are 2D inverse correlation techniques that allow for the determination of connectivity between two different nuclear species. HMQC is selective for direct coupling and HMBC gives longer range couplings (2-4 bond coupling).

See also

- Exclusive correlation spectroscopy
- Two dimensional correlation analysis

User:Bci2/2D-FT NMRI and Spectroscopy

2D-FT Nuclear Magnetic resonance imaging (2D-FT NMRI), or **Two-dimensional Fourier transform** magnetic resonance imaging (**NMRI**), is primarily a non-invasive imaging technique most commonly used in biomedical research and medical radiology/nuclear medicine/MRI to visualize structures and functions of the living systems and single cells. For example it can provides fairly detailed images of a human body in any selected cross-sectional plane, such as longitudinal, transversal, sagital, etc. NMRI provides much greater contrast especially for the different soft tissues of the body than computed tomography (CT) as its most sensitive option observes the nuclear spin distribution and dynamics of highly mobile molecules that contain the naturally abundant, stable hydrogen isotope ^1H as in plasma water molecules, blood, disolved metabolites and fats. This approach makes it most useful in cardiovascular, oncological (cancer), neurological (brain), musculoskeletal, and cartilage imaging. Unlike CT, it uses no ionizing radiation, and also unlike nuclear imaging it does not employ any radioactive isotopes. Some of the first MRI images reported were published in 1973^[1] and the first study performed on a human took place on July 3, 1977.^[2] Earlier papers were also published by Peter Mansfield^[3] in UK (Nobel Laureate in 2003), and R. Damadian in the USA, (together with an approved patent for magnetic imaging). Unpublished 'high-resolution' (50 micron resolution) images of other living systems, such as hydrated wheat grains, were obtained and communicated in UK in 1977-1979, and were subsequently confirmed by articles published in *Nature*.

NMRI Principle

Certain nuclei such as ^1H nuclei, or 'fermions' have spin-1/2, because there are two spin states, referred to as "up" and "down" states. The nuclear magnetic resonance absorption phenomenon occurs when samples containing such nuclear spins are placed in a static magnetic field and a very short radiofrequency pulse is applied with a center, or carrier, frequency matching that of the transition between the up and down states of the spin-1/2 ^1H nuclei that were polarized by the static magnetic field. [4] Very low field schemes have also been recently reported. [5]



Advanced clinical diagnostics and biomedical research NMR Imaging instrument.

Chemical Shifts

NMR is a very useful family of techniques for chemical and biochemical research because of the chemical shift; this effect consists in a frequency shift of the nuclear magnetic resonance for specific chemical groups or atoms as a result of the partial shielding of the corresponding nuclei from the applied, static external magnetic field by the electron orbitals (or molecular orbitals) surrounding such nuclei present in the chemical groups. Thus, the higher the electron density surrounding a specific nucleus the larger the chemical shift will be. The resulting magnetic field at the nucleus is thus lower than the applied external magnetic field and the resonance frequencies observed as a result of such shielding are lower than the value that would be observed in the absence of any electronic orbital shielding. Furthermore, in order to obtain a chemical shift value independent of the strength of the applied magnetic field and allow for the direct comparison of spectra obtained at different magnetic field values, the chemical shift is defined by the ratio of the strength of the local magnetic field value at the observed (electron orbital-shielded) nucleus by the external magnetic field strength, H_{loc} / H_0 . The first NMR observations of the chemical shift, with the correct physical chemistry interpretation, were reported for ^{19}F containing compounds in the early 1950's by Herbert S. Gutowsky and Charles P. Slichter from the University of Illinois at Urbana (USA).

NMR Imaging Principles

A number of methods have been devised for combining magnetic field gradients and radiofrequency pulsed excitation to obtain an image. Two major methods involve either 2D -FT or 3D-FT^[6] reconstruction from projections, somewhat similar to Computed Tomography, with the exception of the image interpretation that in the former case must include dynamic and relaxation/contrast enhancement information as well. Other schemes involve building the NMR image either point-by-point or line-by-line. Some schemes use instead gradients in the rf field rather than in the static magnetic field. The majority of NMR images routinely obtained are either by the Two-Dimensional Fourier Transform (2D-FT) technique ^[7] (with slice selection), or by the Three-Dimensional Fourier Transform (3D-FT) techniques that are however much more time consuming at present. 2D-FT NMRI is sometime called in common parlance a "spin-warp". An NMR image corresponds to a spectrum consisting of a number of 'spatial frequencies' at different locations in the sample investigated, or in a patient. ^[8] A two-dimensional

Fourier transformation of such a "real" image may be considered as a representation of such "real waves" by a matrix of spatial frequencies known as the k -space. We shall see next in some mathematical detail how the 2D-FT computation works to obtain 2D-FT NMR images.

Two-dimensional Fourier transform imaging and spectroscopy

A two-dimensional Fourier transform (2D-FT) is computed numerically or carried out in two stages, both involving 'standard', one-dimensional Fourier transforms. However, the second stage Fourier transform is not the inverse Fourier transform (which would result in the original function that was transformed at the first stage), but a Fourier transform in a second variable-- which is 'shifted' in value-- relative to that involved in the result of the first Fourier transform. Such 2D-FT analysis is a very powerful method for both NMRI and two-dimensional nuclear magnetic resonance spectroscopy (2D-FT NMRS)^[9] that allows the three-dimensional reconstruction of polymer and biopolymer structures at atomic resolution[]].^[10] for molecular weights (Mw) of dissolved biopolymers in aqueous solutions (for example) up to about 50,000 Mw. For larger biopolymers or polymers, more complex methods have been developed to obtain limited structural resolution needed for partial 3D-reconstructions of higher molecular structures, e.g. for up 900,000 Mw or even oriented microcrystals in aqueous suspensions or single crystals; such methods have also been reported for *in vivo* 2D-FT NMR spectroscopic studies of algae, bacteria, yeast and certain mammalian cells, including human ones. The 2D-FT method is also widely utilized in optical spectroscopy, such as *2D-FT NIR hyperspectral imaging* (2D-FT NIR-HS), or in MRI imaging for research and clinical, diagnostic applications in Medicine. In the latter case, 2D-FT NIR-HS has recently allowed the identification of single, malignant cancer cells surrounded by healthy human breast tissue at about 1 micron resolution, well-beyond the resolution obtainable 2D-FT NMRI for such systems in the limited time available for such diagnostic investigations (and also in magnetic fields up to the FDA approved magnetic field strength H_0 of 4.7 T, as shown in the top image of the state-of-the-art NMRI instrument). A more precise mathematical definition of the 'double' (2D) Fourier transform involved in both 2D NMRI and 2D-FT NMRS is specified next, and a precise example follows this generally accepted definition.

2D-FT Definition

A *2D-FT*, or *two-dimensional Fourier transform*, is a standard Fourier transformation of a function of two variables, $f(x_1, x_2)$, carried first in the first variable x_1 , followed by the Fourier transform in the second variable x_2 of the resulting function $F(s_1, x_2)$. Note that in the case of both 2D-FT NMRI and 2D-FT NMRS the two independent variables in this definition are in the time domain, whereas the results of the two successive Fourier transforms have, of course, frequencies as the independent variable in the NMRS, and ultimately spatial coordinates for both 2D NMRI and 2D-FT NMRS following computer structural reconstructions based on special algorithms that are different from FT or 2D-FT. Moreover, such structural algorithms are different for 2D NMRI and 2D-FT NMRS: in the former case they involve macroscopic, or anatomical structure determination, whereas in the latter case of 2D-FT NMRS the atomic structure reconstruction algorithms are based on the quantum theory of a microphysical (quantum) process such as nuclear Overhauser enhancement NOE, or specific magnetic dipole-dipole interactions^[11] between neighbor nuclei.

Example 1

A 2D Fourier transformation and phase correction is applied to a set of 2D NMR (FID) signals : $s(t_1, t_2)$ yielding a real 2D-FT NMR 'spectrum' (collection of 1D FT-NMR spectra) represented by a matrix S whose elements are

$$S(\nu_1, \nu_2) = \text{Re} \int \int \cos(\nu_1 t_1) \exp(-i\nu_2 t_2) s(t_1, t_2) dt_1 dt_2$$

where : ν_1 and : ν_2 denote the discrete indirect double-quantum and single-quantum(detection) axes, respectively, in the 2D NMR experiments. Next, the \emph{covariance matrix} is calculated in the frequency domain according to the following equation

$$C(\nu'_2, \nu_2) = S^T S = \sum_{\nu_1} [S(\nu_1, \nu'_2) S(\nu_1, \nu_2)], \text{ with : } \nu_2, \nu'_2 \text{ taking all possible single-quantum frequency values and with the summation carried out over all discrete, double quantum frequencies : } \nu_1.$$

Example 2

Atomic Structure from 2D-FT STEM Images ^[12] of electron distributions in a high-temperature cuprate superconductor 'paracrystal' reveal both the domains (or 'location') and the local symmetry of the 'pseudo-gap' in the electron-pair correlation band responsible for the high-temperature superconductivity effect (obtained at Cornell University). So far there have been three Nobel prizes awarded for 2D-FT NMR/MRI during 1992-2003, and an additional, earlier Nobel prize for 2D-FT of X-ray data ('CAT scans'); recently the advanced possibilities of 2D-FT techniques in Chemistry, Physiology and Medicine ^[13] received very significant recognition. ^[14]

Brief explanation of NMRI diagnostic uses in Pathology

As an example, a diseased tissue such as a malign tumor, can be detected by 2D-FT NMRI because the hydrogen nuclei of molecules in different tissues return to their equilibrium spin state at different relaxation rates, and also because of the manner in which a malign tumor spreads and grows rapidly along the blood vessels adjacent to the tumor, also inducing further vascularization to occur. By changing the pulse delays in the RF pulse sequence employed, and/or the RF pulse sequence itself, one may obtain a 'relaxation-based contrast', or contrast enhancement between different types of body tissue, such as normal vs. diseased tissue cells for example. Excluded from such diagnostic observations by NMRI are all patients with ferromagnetic metal implants, (e.g., cochlear implants), and all cardiac pacemaker patients who cannot undergo any NMRI scan because of the very intense magnetic and RF fields employed in NMRI which would strongly interfere with the correct functioning of such pacemakers. It is, however, conceivable that future developments may also include along with the NMRI diagnostic treatments with special techniques involving applied magnetic fields and very high frequency RF. Already, surgery with special tools is being experimented on in the presence of NMR imaging of subjects. Thus, NMRI is used to image almost every part of the body, and is especially useful for diagnosis in neurological conditions, disorders of the muscles and joints, for evaluating tumors, such as in lung or skin cancers, abnormalities in the heart (especially in children with hereditary disorders), blood vessels, CAD, atherosclerosis and cardiac infarcts ^[15] (courtesy of Dr. Robert R. Edelman)

See also

- Nuclear magnetic resonance (NMR)
- Medical imaging
- Protein nuclear magnetic resonance spectroscopy
- Kurt Wüthrich
- Chemical shift
- Computed tomography (CT)
- Fourier transform spectroscopy (FTS)
- Richard R. Ernst
- Magnetic resonance microscopy
- Solid-state NMR
- Herbert S. Gutowsky
- John S. Waugh
- Charles P. Slichter
- FT-NIRS (NIR)
- Magnetic resonance elastography
- Relaxation
- Earth's field NMR (EFNMR)
- Robinson oscillator

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External links

- Cardiac Infarct or "heart attack" Imaged in Real Time by 2D-FT NMRI (http://www.mr-tip.com/exam_gifs/cardiac_infarct_short_axis_cine_6.gif)
- 3D Animation Movie about MRI Exam (<http://www.patienccys.com/MRI/>)
- Interactive Flash Animation on MRI (<http://www.e-mri.org>) - *Online Magnetic Resonance Imaging physics and technique course*
- International Society for Magnetic Resonance in Medicine (<http://www.ismrm.org>)
- Danger of objects flying into the scanner (http://www.simplyphysics.com/flying_objects.html)

Related Wikipedia websites

- Medical imaging
- Computed tomography
- Magnetic resonance microscopy
- Fourier transform spectroscopy
- FT-NIRS
- Magnetic resonance elastography
- Nuclear magnetic resonance (NMR)
- Chemical shift
- Relaxation
- Robinson oscillator
- Earth's field NMR (EFNMR)
- Rabi cycle

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Solid-state nuclear magnetic resonance

Solid-state NMR (SSNMR) spectroscopy is a kind of nuclear magnetic resonance (NMR) spectroscopy, characterized by the presence of anisotropic (directionally dependent) interactions.

Introduction

Basic concepts A spin interacts with a magnetic or an electric field. Spatial proximity and/or a chemical bond between two atoms can give rise to interactions between nuclei. In general, these interactions are orientation dependent. In media with no or little mobility (e.g. crystals, powders, large membrane vesicles, molecular aggregates), anisotropic interactions have a substantial influence on the behaviour of a system of nuclear spins.

In contrast, in a classical liquid-state NMR experiment, Brownian motion leads to an averaging of anisotropic interactions. In such cases, these interactions can be neglected on the time-scale of the NMR experiment.

Examples of anisotropic nuclear interactions Two directionally dependent interactions commonly found in solid-state NMR are the *chemical shift anisotropy* (CSA) and the internuclear *dipolar coupling*. Many more such interactions exist, such as the anisotropic J-coupling in NMR, or in related fields, such as the *g*-tensor in electron spin resonance. In mathematical terms, all these interactions can be described using the same formalism.

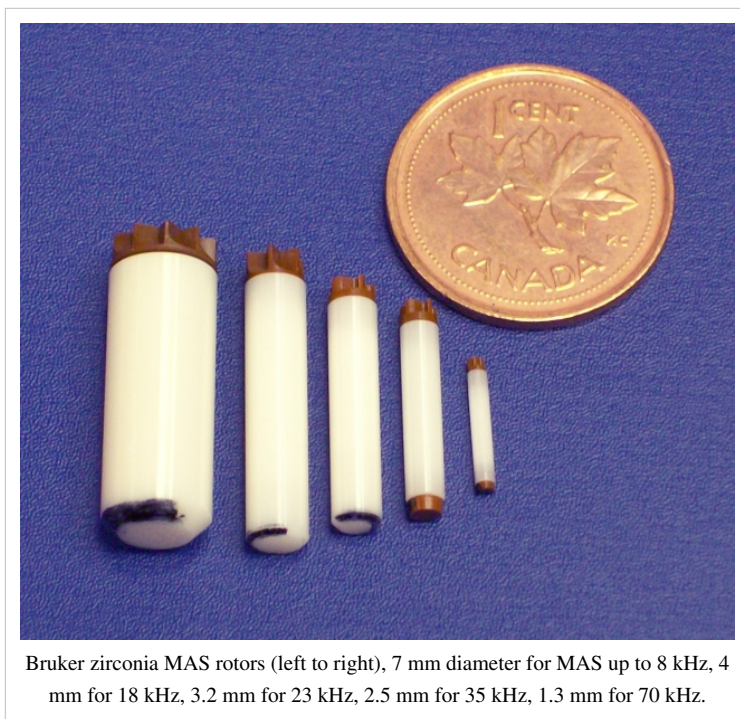


Solid-state 900 MHz ($21.1 \text{ T}^{[1]}$) NMR spectrometer at the Canadian National Ultrahigh-field NMR Facility for Solids.

Experimental background Anisotropic interactions modify the nuclear spin energy levels (and hence the resonance frequency) of all sites in a molecule, and often contribute to a line-broadening effect in NMR spectra. However, there is a range of situations when their presence can either not be avoided, or is even particularly desired, as they encode structural parameters, such as orientation information, on the molecule of interest.

High-resolution conditions in solids (in a wider sense) can be established using magic angle spinning (MAS), macroscopic sample orientation, combinations of both of these techniques, enhancement of mobility by highly viscous sample conditions, and a variety of radio frequency (RF) irradiation patterns. While the latter allows decoupling of interactions in spin space, the others facilitate averaging of interactions in real space. In addition, line-broadening effects from microscopic inhomogeneities can be reduced by appropriate methods of sample preparation.

Under decoupling conditions, isotropic interactions can report on the local structure, e.g. by the isotropic chemical shift. In addition, decoupled interactions can be selectively re-introduced (recoupling"), and used, for example, for controlled de-phasing or transfer of polarization, which allows to derive a number of structural parameters.



Solid-state NMR line widths The residual line width (full width at half max) of ^{13}C nuclei under MAS conditions at 5–15 kHz spinning rate is typically in the order of 0.5–2 ppm, and may be comparable to solution-state NMR conditions. Even at MAS rates of 20 kHz and above, however, non linear groups (not a straight line) of the same nuclei linked via the homonuclear dipolar interactions can only be suppressed partially, leading to line widths of 0.5 ppm and above, which is considerably more than in optimal solution state NMR conditions. Other interactions such as the quadrupolar interaction can lead to line widths of 1000's of ppm due to the strength of the interaction. The first-order quadrupolar broadening is largely suppressed by sufficiently fast MAS, but the second-order quadrupolar broadening has a different angular dependence and cannot be removed by spinning at one angle alone. Ways to achieve isotropic lineshapes for quadrupolar nuclei include spinning at two angles simultaneously (DOR), sequentially (DAS), or through refocusing the second-order quadrupolar interaction with a two-dimensional experiment such as MQMAS or STMAS.

Anisotropic interactions in solution-state NMR From the perspective of solution-state NMR, it can be desirable to reduce motional averaging of dipolar interactions by alignment media. The order of magnitude of these residual dipolar couplings (RDCs) are typically of only a few rad/Hz, but do not destroy high-resolution conditions, and provide a pool of information, in particular on the orientation of molecular domains with respect to each other.

Dipolar truncation The dipolar coupling between two nuclei is inversely proportional to the cube of their distance. This has the effect that the polarization transfer mediated by the dipolar interaction is cut off in the presence of a third nucleus (all of the same kind, e.g. ^{13}C) close to one of these nuclei. This effect is commonly referred to as dipolar truncation. It has been one of the major obstacles in efficient extraction of internuclear distances, which are crucial in the structural analysis of biomolecular structure. By means of labeling schemes or pulse sequences, however, it has become possible to circumvent this problem in a number of ways.

Nuclear spin interactions in the solid phase

Chemical shielding

The chemical shielding is a local property of each nucleus, and depends on the external magnetic field.

Specifically, the external magnetic field induces currents of the electrons in molecular orbitals. These induced currents create local magnetic fields that often vary across the entire molecular framework such that nuclei in distinct molecular environments usually experience unique local fields from this effect.

Under sufficiently fast magic angle spinning, or in solution-state NMR, the directionally dependent character of the chemical shielding is removed, leaving the isotropic chemical shift.

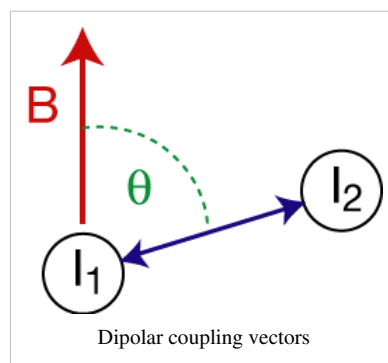
J-coupling

The J-coupling or indirect nuclear spin-spin coupling (sometimes also called "scalar" coupling despite the fact that $\mathbf{J}$ is a tensor quantity) describes the interaction of nuclear spins through chemical bonds.

Dipolar coupling

Main article: Dipolar coupling (NMR)

Nuclear spins exhibit a dipole moment, which interacts with the dipole moment of other nuclei (dipolar coupling). The magnitude of the interaction is dependent on the spin species, the internuclear distance, and the orientation of the vector connecting the two nuclear spins with respect to the external magnetic field B (see figure). The maximum dipolar coupling is given by the dipolar coupling constant d ,



$$d = \frac{\hbar \mu_0}{4\pi} \frac{\gamma_1 \gamma_2}{r^3},$$

where r is the distance between the nuclei, and γ_1 and γ_2 are the gyromagnetic ratios of the nuclei. In a strong magnetic field, the dipolar coupling depends on the orientation of the internuclear vector with the external magnetic field by

$$D \propto 3 \cos^2 \theta - 1.$$

Consequently, two nuclei with a dipolar coupling vector at an angle of $\theta_m = 54.7^\circ$ to a strong external magnetic field, which is the angle where D becomes zero, have zero dipolar coupling. θ_m is called the magic angle. One technique for removing dipolar couplings, at least to some extent, is magic angle spinning.

Quadrupolar interaction

Nuclei with a spin greater than one-half have a non spherical charge distribution. This is known as a quadrupolar nucleus. A non spherical charge distribution can interact with an electric field gradient caused by some form of non-symmetry (e.g. in a trigonal bonding atom there are electrons around it in a plane, but not above or below it) to produce a change in the energy level in addition to the Zeeman effect. The quadrupolar interaction is the largest interaction in NMR apart from the Zeeman interaction and they can even become comparable in size. Due to the interaction being so large it can not be treated to just the first order, like most of the other interactions. This means you have a first and second order interaction, which can be treated separately. The first order interaction has an angular dependency with respect to the magnetic field of $(3 \cos^2 \theta - 1)$ (the P2 Legendre polynomial), this means

that if you spin the sample at $\theta = \arctan \sqrt{2} (\sim 54.74^\circ)$ you can average out the first order interaction over one rotor period (all other interactions apart from Zeeman, Chemical shift, paramagnetic and J coupling also have this angular dependency). However, the second order interaction depends on the P4 Legendre polynomial which has zero points at 30.6° and 70.1° . These can be taken advantage of by either using DOR (DOuble angle Rotation) where you spin at two angles at the same time, or DAS (Double Angle Spinning) where you switch quickly between the two angles. But these techniques suffer from the fact that they require special hardware (probe). A revolutionary advance is Lucio Frydman's multiple quantum magic angle spinning (MQMAS) NMR in 1995 and it has become a routine method for obtaining high resolution solid-state NMR spectra of quadrupolar nuclei^{[2] [3]}. A similar method to MQMAS is satellite transition magic angle spinning (STMAS) NMR proposed by Zhehong Gan in 2000.

Other interactions

Paramagnetic substances are subject to the Knight shift.

History

See also: nuclear magnetic resonance or NMR spectroscopy articles for an account on discoveries in NMR and NMR spectroscopy in general.

History of discoveries of NMR phenomena, and the development of solid-state NMR spectroscopy:

Purcell, Torrey and Pound: "nuclear induction" on ^1H in paraffin 1945, at about the same time Bloch *et al.* on ^1H in water.

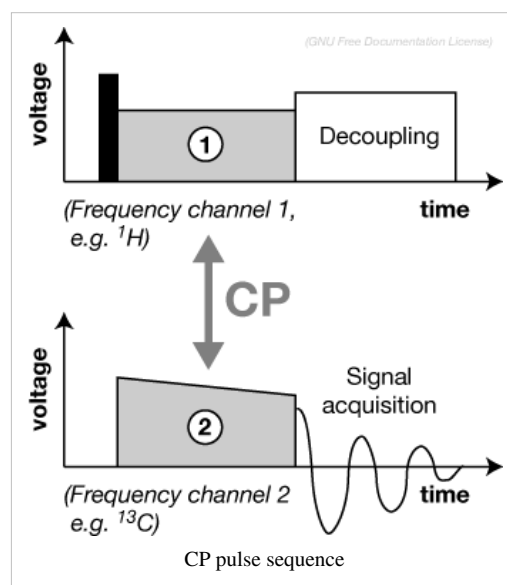
Modern solid-state NMR spectroscopy

Methods and techniques

Basic example

A fundamental RF pulse sequence and building-block in most solid-state NMR experiments is cross-polarization (CP) [Waugh *et al.*]. It can be used to enhance the signal of nuclei with a low gyromagnetic ratio (e.g. ^{13}C , ^{15}N) by magnetization transfer from nuclei with a high gyromagnetic ratio (e.g. ^1H), or as spectral editing method (e.g. directed $^{15}\text{N} \rightarrow ^{13}\text{C}$ CP in protein spectroscopy). In order to establish magnetization transfer, the RF pulses applied on the two frequency channels must fulfill the Hartmann–Hahn condition [Hartmann, 1962]. Under MAS, this condition defines a relationship between the voltage through the RF coil and the rate of sample rotation. Experimental optimization of such conditions is one of the routine tasks in performing a (solid-state) NMR experiment.

CP is a basic building block of most pulse sequences in solid-state NMR spectroscopy. Given its importance, a pulse sequence employing direct excitation of ^1H spin polarization, followed by CP transfer to and signal detection of ^{13}C , ^{15}N or similar nuclei, is itself often referred to as *CP experiment*, or, in conjunction with MAS, as *CP-MAS* [Schaefer and Stejskal, 1976]. It is the typical starting point of an investigation using solid-state NMR spectroscopy.



Decoupling

Nuclear spin interactions need to be removed (decoupled) in order to increase the resolution of NMR spectra, and to isolate spin systems.

A technique that can substantially reduce or remove the chemical shift anisotropy, the dipolar coupling is *sample rotation* (most commonly magic angle spinning, but also off-magic angle spinning).

Homonuclear RF decoupling decouples spin interactions of nuclei which are the same as those which are being detected. *Heteronuclear RF decoupling* decouples spin interactions of other nuclei.

Recoupling

Although the broadened lines are often not desired, dipolar couplings between atoms in the crystal lattice can also provide very useful information. Dipolar coupling are distance dependent, and so they may be used to calculate interatomic distances in isotopically labeled molecules.

Because most dipolar interactions are removed by sample spinning, recoupling experiments are needed to re-introduce desired dipolar couplings so they can be measured.

An example of a recoupling experiment is the Rotational Echo DOuble Resonance (REDOR) experiment [Gullion and Schaefer, 1989].

Applications

Biology

Membrane proteins and amyloid fibrils, the latter related to Alzheimer's disease and Parkinson's disease, are two examples of application where solid-state NMR spectroscopy complements solution-state NMR spectroscopy and beam diffraction methods (e.g. X-ray crystallography, electron microscopy).

Chemistry

Solid-state NMR spectroscopy serves as an analysis tool in organic and inorganic chemistry. SSNMR is also a valuable tool to study local dynamics, kinetics, and thermodynamics of a variety of systems.

References

- [1] http://nmr900.ca/instrument_e.html
- [2] Isotropic Spectra of Half-Integer Quadrupolar Spins from Bidimensional Magic-Angle Spinning NMR, Lucio Frydman and John S. Hardwood, *J. Am. Chem. Soc.*, **1995**, *117*, 5367—5368, (1995)
- [3] Two-dimensional Magic-Angle Spinning Isotropic Reconstruction Sequences for Quadrupolar Nuclei, D. Massiot, B. Touzo, D. Trumeau, J. P. Coutures, J. Virlet, P. Florian and P. J. Grandinetti, *Solid-State NMR*, **6**, 73 (1996)

Suggested readings for beginners

- High Resolution Solid-State NMR of Quadrupolar Nuclei (<http://www.grandinetti.org/assets/GrandinettiRMCBruker2007.pdf>) Grandinetti ENC Tutorial
- David D. Laws, Hans-Marcus L. Bitter, and Alexej Jerschow, "Solid-State NMR Spectroscopic Methods in Chemistry", *Angewandte Chemie International Edition (engl.)*, Vol. 41, pp. 3096 (2002)
doi:10.1002/1521-3773(20020902)41:17<3096::AID-ANIE3096>3.0.CO;2-X
- Levitt, Malcolm H., *Spin Dynamics: Basics of Nuclear Magnetic Resonance*, Wiley, Chichester, United Kingdom, 2001. (NMR basics, including solids)
- Duer, Melinda J., *Introduction to Solid-State NMR Spectroscopy*, Blackwell, Oxford, 2004. (Some detailed examples of SSNMR spectroscopy)

Advanced readings

Books and major review articles

- McDermott, A, Structure and Dynamics of Membrane Proteins by Magic Angle Spinning Solid-State NMR (<http://arjournals.annualreviews.org/doi/abs/10.1146/annurev.biophys.050708.133719>) *Annual Review of Biophysics*, v. 38, 2009.
- Mehring, M, *Principles of High Resolution NMR in Solids*, 2nd ed., Springer, Heidelberg, 1983.
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General

References to books and research articles

- Andrew, E. R., Bradbury, A. and Eades, R. G., "Removal of Dipolar Broadening of Nuclear Magnetic Resonance Spectra of Solids by Specimen Rotation," *Nature* 183, 1802, (1959)
- Ernst, Bodenhausen, Wokaun: *Principles of Nuclear Magnetic Resonance in One and Two Dimensions*
- Hartmann S.R., Hahn E.L., "Nuclear Double Resonance in the Rotating Frame" *Phys. Rev.* 128 (1962) 2042.
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- Purcell, Torrey and Pound (1945).
- Schaefer, J. and Stejskal, E. O., "Carbon-13 Nuclear Magnetic Resonance of Polymers Spinning at the Magic Angle," *Journal of the American Chemical Society* 98, 1031 (1976).
- Gullion, T. and Schaefer, J., "Rotational-Echo, Double-Resonance NMR," *J. Magn. Reson.*, 81, 196 (1989).

External links

- NMRWiki.ORG (<http://www.nmrwiki.org>) NMR resource you can edit
 - SSNMRBLOG (<http://ssnmr.blogspot.com/>) Solid-State NMR Literature Blog by Prof. Rob Schurko's Solid-State NMR group at the University of Windsor
 - www.ssnmr.org (<http://www.ssnmr.org>) Rocky Mountain Conference on Solid-State NMR
 - Varian Inc (<http://www.varianinc.com>) NMR system/product manufacturer
-

Magnetic resonance microscopy

Magnetic Resonance Microscopy (MRM, μ MRI) is Magnetic Resonance Imaging (MRI) at a microscopic level. A strict definition is MRI having voxel resolutions of better than $100\text{ }\mu\text{m}^3$ ^[1].

Nomenclature

Many scientist in the field consider the name Magnetic Resonance Microscopy to be a misnomer, since the images produced are much worse than those produced by even a marginal optical or electron microscope. As such, the name High Resolution Magnetic Resonance Imaging is often preferred in scientific literature on the subject. In fact, the term is most widely used by the High Resolution Magnetic Resonance Imaging group from Duke University, headed by Allan Johnson.

Differences between MRI and MRM

- Resolution: Typical medical MRI resolution is about 1 mm^3 ; the desired resolution of MRM is $100\text{ }\mu\text{m}^3$ or smaller.
- Specimen size: Medical MRI machines are designed so that a patient may fit inside. MRM chambers are usually small, typically less than 1 cm^3 .

Current status of MRM

Although MRI is very common for medical applications, MRM is still developed in laboratories. The major barriers for practical MRM include:

- Magnetic field gradient: High gradient focus the magnetic resonance in a smaller volume (smaller point spread function), results in a better spatial resolution. The gradients for MRM are typically 50 to 100 times those of clinical systems. However, the construction of radio frequency (RF) coil used in MRM does not allow ultrahigh gradient.
- Sensitivity: Because the voxels for MRM can be $1/100,000$ of those in MRI, the signal will be proportionately weaker ^[2].

Alternative MRM

Magnetic Resonance Force Microscopy (MRFM) is claimed to have nm^3 -scale resolutions. It improves the sensitivity issue by introducing microfabricated cantilever to measure tiny signals. The magnetic gradient is generated by a micrometre-scale magnetic tip, yielding a typical gradient 10 million times larger than those of clinical systems. This technique is still in the beginning stage. Because the specimen need to be in high vacuum at cryogenic temperatures, MRFM can be only used for solid state matters.

External links

- Introduction to Magnetic Resonance Microscopy ^[3] Auditory Research Laboratory at the Univ. of North Carolina.

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- [2] R. Maronpot Applications of Magnetic Resonance Microscopy, Toxicologic Pathology, 32(Suppl. 2):42–48, 2004
- [3] http://cbaweb2.med.unc.edu/henson_mrm/pages/mrmfaq.html#MRMAAnchor

Imaging

Medical imaging

Medical imaging is the technique and process used to create images of the human body (or parts and function thereof) for clinical purposes (medical procedures seeking to reveal, diagnose or examine disease) or medical science (including the study of normal anatomy and physiology). Although imaging of removed organs and tissues can be performed for medical reasons, such procedures are not usually referred to as medical imaging, but rather are a part of pathology.

As a discipline and in its widest sense, it is part of biological imaging and incorporates radiology (in the wider sense), nuclear medicine, investigative radiological sciences, endoscopy, (medical) thermography, medical photography and microscopy (e.g. for human pathological investigations).

Measurement and recording techniques which are not primarily designed to produce images, such as electroencephalography (EEG), magnetoencephalography (MEG), Electrocardiography (EKG) and others, but which produce data susceptible to be represented as maps (i.e. containing positional information), can be seen as forms of medical imaging.

Overview

In the clinical context, medical imaging is generally equated to radiology or "clinical imaging" and the medical practitioner responsible for interpreting (and sometimes acquiring) the images is a radiologist. Diagnostic radiography designates the technical aspects of medical imaging and in particular the acquisition of medical images. The *radiographer* or *radiologic technologist* is usually responsible for acquiring medical images of diagnostic quality, although some radiological interventions are performed by radiologists. While radiology is an evaluation of anatomy, nuclear medicine provides functional assessment.

As a field of scientific investigation, medical imaging constitutes a sub-discipline of biomedical engineering, medical physics or medicine depending on the context: Research and development in the area of instrumentation, image acquisition (e.g. radiography), modelling and quantification are usually the preserve of biomedical engineering, medical physics and computer science; Research into the application and interpretation of medical images is usually the preserve of radiology and the medical sub-discipline relevant to medical condition or area of medical science (neuroscience, cardiology, psychiatry, psychology, etc.) under investigation. Many of the techniques developed for medical imaging also have scientific and industrial applications.

Medical imaging is often perceived to designate the set of techniques that noninvasively produce images of the internal aspect of the body. In this restricted sense, medical imaging can be seen as the solution of mathematical inverse problems. This means that cause (the properties of living tissue) is inferred from effect (the observed signal). In the case of ultrasonography the probe consists of ultrasonic pressure waves and echoes inside the tissue show the internal structure. In the case of projection radiography, the probe is X-ray radiation which is absorbed at different rates in different tissue types such as bone, muscle and fat.

The term noninvasive is a term based on the fact that following medical imaging modalities do not penetrate the skin physically. But on the electromagnetic and radiation level, they are quite invasive. From the high energy photons in X-Ray Computed Tomography, to the 2+ Tesla coils of an MRI device, these modalities alter the physical and chemical reactions of the body in order to obtain data.

Radiography

Two forms of radiographic images are in use in medical imaging; projection radiography and fluoroscopy, with the latter being useful for intraoperative and catheter guidance. These 2D techniques are still in wide use despite the advance of 3D tomography due to the low cost, high resolution, and depending on application, lower radiation dosages. This imaging modality utilizes a wide beam of x rays for image acquisition and is the first imaging technique available in modern medicine.

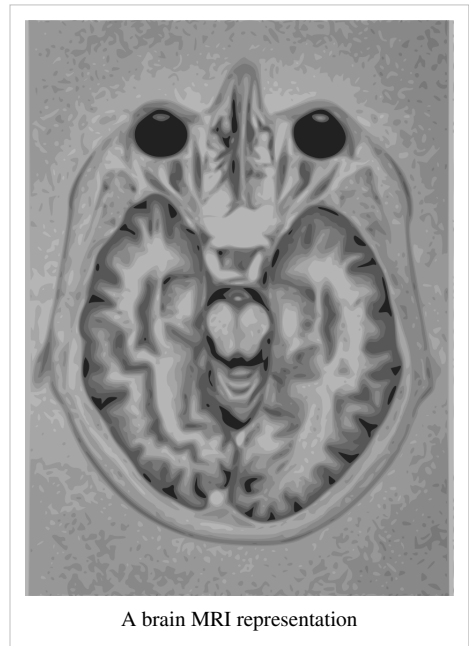
- *Fluoroscopy* produces real-time images of internal structures of the body in a similar fashion to radiography, but employs a constant input of x-rays, at a lower dose rate. Contrast media, such as barium, iodine, and air are used to visualize internal organs as they work. Fluoroscopy is also used in image-guided procedures when constant feedback during a procedure is required. An image receptor is required to convert the radiation into an image after it has passed through the area of interest. Early on this was a fluorescing screen, which gave way to an Image Amplifier (IA) which was a large vacuum tube that had the receiving end coated with cesium iodide, and a mirror at the opposite end. Eventually the mirror was replaced with a TV camera.
- *Projectional radiographs*, more commonly known as x-rays, are often used to determine the type and extent of a fracture as well as for detecting pathological changes in the lungs. With the use of radio-opaque contrast media, such as barium, they can also be used to visualize the structure of the stomach and intestines - this can help diagnose ulcers or certain types of colon cancer.

Magnetic resonance imaging (MRI)

A magnetic resonance imaging instrument (MRI scanner), or "nuclear magnetic resonance (NMR) imaging" scanner as it was originally known, uses powerful magnets to polarise and excite hydrogen nuclei (single proton) in water molecules in human tissue, producing a detectable signal which is spatially encoded, resulting in images of the body. MRI uses three electromagnetic fields: a very strong (on the order of units of teslas) static magnetic field to polarize the hydrogen nuclei, called the static field; a weaker time-varying (on the order of 1 kHz) field(s) for spatial encoding, called the gradient field(s); and a weak radio-frequency (RF) field for manipulation of the hydrogen nuclei to produce measurable signals, collected through an RF antenna.

Like CT, MRI traditionally creates a two dimensional image of a thin "slice" of the body and is therefore considered a tomographic imaging technique. Modern MRI instruments are capable of producing images in the form of 3D blocks, which may be considered a generalisation of the single-slice, tomographic, concept. Unlike CT, MRI does not involve the use of ionizing radiation and is therefore not associated with the same health hazards. For example, because MRI has only been in use since the early 1980s, there are no known long-term effects of exposure to strong static fields (this is the subject of some debate; see 'Safety' in MRI) and therefore there is no limit to the number of scans to which an individual can be subjected, in contrast with X-ray and CT. However, there are well-identified health risks associated with tissue heating from exposure to the RF field and the presence of implanted devices in the body, such as pace makers. These risks are strictly controlled as part of the design of the instrument and the scanning protocols used.

Because CT and MRI are sensitive to different tissue properties, the appearance of the images obtained with the two techniques differ markedly. In CT, X-rays must be blocked by some form of dense tissue to create an image, so the image quality when looking at soft tissues will be poor. In MRI, while any nucleus with a net nuclear spin can be



A brain MRI representation

used, the proton of the hydrogen atom remains the most widely used, especially in the clinical setting, because it is so ubiquitous and returns a large signal. This nucleus, present in water molecules, allows the excellent soft-tissue contrast achievable with MRI.

Nuclear medicine

Nuclear medicine encompasses both diagnostic imaging and treatment of disease, and may also be referred to as molecular medicine or molecular imaging & therapeutics^[1]. Nuclear medicine uses certain properties of isotopes and the energetic particles emitted from radioactive material to diagnose or treat various pathology. Different from the typical concept of anatomic radiology, nuclear medicine enables assessment of physiology. This function-based approach to medical evaluation has useful applications in most subspecialties, notably oncology, neurology, and cardiology. *Gamma cameras* are used in e.g. scintigraphy, SPECT and PET to detect regions of biologic activity that may be associated with disease. Relatively short lived isotope, such as ^{123}I is administered to the patient. Isotopes are often preferentially absorbed by biologically active tissue in the body, and can be used to identify tumors or fracture points in bone. Images are acquired after collimated photons are detected by a crystal that gives off a light signal, which is in turn amplified and converted into count data.

- *Scintigraphy* ("scint") is a form of diagnostic test wherein radioisotopes are taken internally, for example intravenously or orally. Then, gamma camera capture and form two-dimensional^[2] images from the radiation emitted by the radiopharmaceuticals. For example, technetium-labeled isoniazid (INH) and ethambutol (EMB) has been used for tubercular imaging for early diagnosis of tuberculosis^[3].
 - *SPECT* is a 3D tomographic technique that uses gamma camera data from many projections and can be reconstructed in different planes. A dual detector head gamma camera combined with a CT scanner, which provides localization of functional SPECT data, is termed a SPECT/CT camera, and has shown utility in advancing the field of molecular imaging. In most other medical imaging modalities, energy is passed through the body and the reaction or result is read by detectors. In SPECT imaging, the patient is injected with a radioisotope, most commonly Thallium 201TI, Technetium 99mTC, Iodine 123I, and Gallium 68Ga^[4].
- . The radioactive gamma rays are emitted through the body as the natural decaying process of these isotopes takes place. The emissions of the gamma rays are captured by detectors that surround the body. This essentially means that the human is now the source of the radioactivity, rather than the medical imaging devices such as X-Ray, CT, or Ultrasound.
- *Positron emission tomography* (PET) uses coincidence detection to image functional processes. Short-lived positron emitting isotope, such as ^{18}F , is incorporated with an organic substance such as glucose, creating F18-fluorodeoxyglucose, which can be used as a marker of metabolic utilization. Images of activity distribution throughout the body can show rapidly growing tissue, like tumor, metastasis, or infection. PET images can be viewed in comparison to computed tomography scans to determine an anatomic correlate. Modern scanners combine PET with a CT, or even MRI, to optimize the image reconstruction involved with positron imaging. This is performed on the same equipment without physically moving the patient off of the gantry. The resultant hybrid of functional and anatomic imaging information is a useful tool in non-invasive diagnosis and patient management.

Photoacoustic imaging

Photoacoustic imaging is a recently developed hybrid biomedical imaging modality based on the photoacoustic effect. It combines the advantages of optical absorption contrast with ultrasonic spatial resolution for deep imaging in (optical) diffusive or quasi-diffusive regime. Recent studies have shown that photoacoustic imaging can be used in vivo for tumor angiogenesis monitoring, blood oxygenation mapping, functional brain imaging, and skin melanoma detection, etc.

Breast Thermography

Digital infrared imaging thermography is based on the principle that metabolic activity and vascular circulation in both pre-cancerous tissue and the area surrounding a developing breast cancer is almost always higher than in normal breast tissue. Cancerous tumors require an ever-increasing supply of nutrients and therefore increase circulation to their cells by holding open existing blood vessels, opening dormant vessels, and creating new ones (neoangiogenesis). This process frequently results in an increase in regional surface temperatures of the breast. Digital infrared imaging uses extremely sensitive medical infrared cameras and sophisticated computers to detect, analyze, and produce high-resolution diagnostic images of these temperature variations. Because of DII's sensitivity, these temperature variations may be among the earliest signs of breast cancer and/or a pre-cancerous state of the breast^[5].

Tomography

Tomography is the method of imaging a single plane, or slice, of an object resulting in a tomogram. There are several forms of tomography:

- **Linear tomography:** This is the most basic form of tomography. The X-ray tube moved from point "A" to point "B" above the patient, while the cassette holder (or "bucky") moves simultaneously under the patient from point "B" to point "A." The fulcrum, or pivot point, is set to the area of interest. In this manner, the points above and below the focal plane are blurred out, just as the background is blurred when panning a camera during exposure. No longer carried out and replaced by computed tomography.
- **Poly tomography:** This was a complex form of tomography. With this technique, a number of geometrical movements were programmed, such as hypocycloidal, circular, figure 8, and elliptical. Philips Medical Systems [6] produced one such device called the 'Polytome.' This unit was still in use into the 1990s, as its resulting images for small or difficult physiology, such as the inner ear, was still difficult to image with CTs at that time. As the resolution of CTs got better, this procedure was taken over by the CT.
- **Zonography:** This is a variant of linear tomography, where a limited arc of movement is used. It is still used in some centres for visualising the kidney during an intravenous urogram (IVU).
- **Orthopantomography (OPT or OPG):** The only common tomographic examination in use. This makes use of a complex movement to allow the radiographic examination of the mandible, as if it were a flat bone. It is often referred to as a "Panorex", but this is incorrect, as it is a trademark of a specific company.
- **Computed Tomography (CT), or Computed Axial Tomography (CAT:** A CT scan, also known as a CAT scan), is a helical tomography (latest generation), which traditionally produces a 2D image of the structures in a thin section of the body. It uses X-rays. It has a greater ionizing radiation dose burden than projection radiography; repeated scans must be limited to avoid health effects. CT is based on the same principles as X-Ray projections but in this case, the patient is enclosed in a surrounding ring of detectors assigned with 500-1000 scintillation detectors^[4]

. This being the fourth-generation X-Ray CT scanner geometry. Previously in older generation scanners, the X-Ray beam was paired by a translating source and detector.

Ultrasound

Medical ultrasonography uses high frequency broadband sound waves in the megahertz range that are reflected by tissue to varying degrees to produce (up to 3D) images. This is commonly associated with imaging the fetus in pregnant women. Uses of ultrasound are much broader, however. Other important uses include imaging the abdominal organs, heart, breast, muscles, tendons, arteries and veins. While it may provide less anatomical detail than techniques such as CT or MRI, it has several advantages which make it ideal in numerous situations, in particular that it studies the function of moving structures in real-time, emits no ionizing radiation, and contains speckle that can be used in elastography. Ultrasound is also used as a popular research tool for capturing raw data,

that can be made available through an Ultrasound research interface, for the purpose of tissue characterization and implementation of new image processing techniques. The concepts of ultrasound differ from other medical imaging modalities in the fact that it is operated by the transmission and receipt of sound waves. The high frequency sound waves are sent into the tissue and depending on the composition of the different tissues; the signal will be attenuated and returned at separate intervals. A path of reflected sound waves in a multilayered structure can be defined by an input acoustic impedance(Ultrasound sound wave) and the Reflection and transmission coefficients of the relative structures^[4] . It is very safe to use and does not appear to cause any adverse effects, although information on this is not well documented. It is also relatively inexpensive and quick to perform. Ultrasound scanners can be taken to critically ill patients in intensive care units, avoiding the danger caused while moving the patient to the radiology department. The real time moving image obtained can be used to guide drainage and biopsy procedures. Doppler capabilities on modern scanners allow the blood flow in arteries and veins to be assessed.

Medical imaging topics

Maximizing imaging procedure use

The amount of data obtained in a single MR or CT scan is very extensive. Some of the data that radiologists discard could save patients time and money, while reducing their exposure to radiation and risk of complications from invasive procedures.^[7]

Creation of three-dimensional images

Recently, techniques have been developed to enable CT, MRI and ultrasound scanning software to produce 3D images for the physician.^[8] Traditionally CT and MRI scans produced 2D static output on film. To produce 3D images, many scans are made, then combined by computers to produce a 3D model, which can then be manipulated by the physician. 3D ultrasounds are produced using a somewhat similar technique. In diagnosing disease of the viscera of abdomen,ultrasound is particularly sensitive on imaging of biliary tract,urinary tract and female reproductive organs(ovary,fallopian tubes).As for example,diagnosis of gall stone by dilatation of common bile duct and stone in common bile duct . With the ability to visualize important structures in great detail, 3D visualization methods are a valuable resource for the diagnosis and surgical treatment of many pathologies. It was a key resource for the famous, but ultimately unsuccessful attempt by Singaporean surgeons to separate Iranian twins Ladan and Laleh Bijani in 2003. The 3D equipment was used previously for similar operations with great success.

Other proposed or developed techniques include:

- Diffuse optical tomography
- Elastography
- Electrical impedance tomography
- Optoacoustic imaging
- Ophthalmology
 - A-scan
 - B-scan
 - Corneal topography
 - Optical coherence tomography
 - Scanning laser ophthalmoscopy

Some of these techniques are still at a research stage and not yet used in clinical routines.

Compression of medical images

Medical imaging techniques produce very large amounts of data, especially from CT, MRI and PET modalities. As a result, storage and communications of electronic image data are prohibitive without the use of compression. JPEG 2000 is the state-of-the-art image compression DICOM standard for storage and transmission of medical images. The cost and feasibility of accessing large image data sets over low or various bandwidths are further addressed by use of another DICOM standard, called JPIP, to enable efficient streaming of the JPEG 2000 compressed image data.

Non-diagnostic imaging

Neuroimaging has also been used in experimental circumstances to allow people (especially disabled persons) to control outside devices, acting as a brain computer interface.

Archiving and recording

Used primarily in ultrasound imaging, capturing the image a medical imaging device is required for archiving and telemedicine applications. In most scenarios, a frame grabber is used in order to capture the video signal from the medical device and relay it to a computer for further processing and operations.^[9]

Open source software for medical image analysis

Several open source software packages are available for performing analysis of medical images:

- ImageJ
- 3D Slicer
- ITK
- OsiriX
- GemIdent
- MicroDicom
- FreeSurfer

Use in pharmaceutical clinical trials

Medical imaging has become a major tool in clinical trials since it enables rapid diagnosis with visualization and quantitative assessment.

A typical clinical trial goes through multiple phases and can take up to eight years. Clinical endpoints or outcomes are used to determine whether the therapy is safe and effective. Once a patient reaches the endpoint, he/she is generally excluded from further experimental interaction. Trials that rely solely on clinical endpoints are very costly as they have long durations and tend to need large number of patients.

In contrast to clinical endpoints, surrogate endpoints have been shown to cut down the time required to confirm whether a drug has clinical benefits. Imaging biomarkers (a characteristic that is objectively measured by an imaging technique, which is used as an indicator of pharmacological response to a therapy) and surrogate endpoints have shown to facilitate the use of small group sizes, obtaining quick results with good statistical power.^[10]

Imaging is able to reveal subtle change that is indicative of the progression of therapy that may be missed out by more subjective, traditional approaches. Statistical bias is reduced as the findings are evaluated without any direct patient contact.

For example, measurement of tumour shrinkage is a commonly used surrogate endpoint in solid tumour response evaluation. This allows for faster and more objective assessment of the effects of anticancer drugs. In evaluating the extent of Alzheimer's disease, it is still prevalent to use behavioural and cognitive tests. MRI scans on the entire brain can accurately pinpoint hippocampal atrophy rate while PET scans is able to measure the brain's metabolic activity by measuring regional glucose metabolism.^[10]

An imaging-based trial will usually be made up of three components:

1. A realistic imaging protocol. The protocol is an outline that standardizes (as far as practically possible) the way in which the images are acquired using the various modalities (PET, SPECT, CT, MRI). It covers the specifics in which images are to be stored, processed and evaluated.
2. An imaging centre that is responsible for collecting the images, perform quality control and provide tools for data storage, distribution and analysis. It is important for images acquired at different time points are displayed in a standardised format to maintain the reliability of the evaluation. Certain specialised imaging contract research organizations provide to end medical imaging services, from protocol design and site management through to data quality assurance and image analysis.
3. Clinical sites that recruit patients to generate the images to send back to the imaging centre.

See also

- Preclinical imaging
- Cardiac PET
- Biomedical informatics
- Digital Imaging and Communications in Medicine
- Digital Mammography and PACS
- EMMI European Master in Molecular Imaging
- eMix
- Fotofinder
- Full-body scan
- VoluMedic
- Magnetic field imaging
- Medical examination
- Medical radiography
- Medical test
- Neuroimaging
- Non-invasive (medical)
- PACS
- JPEG 2000 compression
- JPIP streaming
- Pneumoencephalogram
- Radiology information system
- Segmentation (image processing)
- Signal-to-noise ratio
- Society for Imaging Science and Technology
- Tomogram
- Virtopsy

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- *Journal of Digital Imaging* (New York: Springer Science+Business Media). ISSN 0897-1889.
- Using JPIP for Standard-Compliant Sharing of Medical Image Data ^[12] a white paper by Aware Inc. ^[13]

External links

- Medical imaging ^[14] at the Open Directory Project
- Medical Image Database ^[15] Free Indexed Online Images
- <http://www.aware.com/imaging/accuradjpip.htm> What is JPIP?

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MRI

Magnetic resonance imaging (MRI), or **nuclear magnetic resonance imaging (NMRI)**, is primarily a noninvasive medical imaging technique used in radiology to visualize detailed internal structure and limited function of the body. MRI provides much greater contrast between the different soft tissues of the body than computed tomography (CT) does, making it especially useful in neurological (brain), musculoskeletal, cardiovascular, and oncological (cancer) imaging.

Unlike CT, MRI uses no ionizing radiation. Rather, it uses a powerful magnetic field to align the nuclear magnetization of (usually) hydrogen atoms in water in the body. Radio frequency (RF) fields are used to systematically alter the alignment of this magnetization. This causes the hydrogen nuclei to produce a rotating magnetic field detectable by the scanner. This signal can be manipulated by additional magnetic fields to build up enough information to construct an image of the body.^{[1]:36}

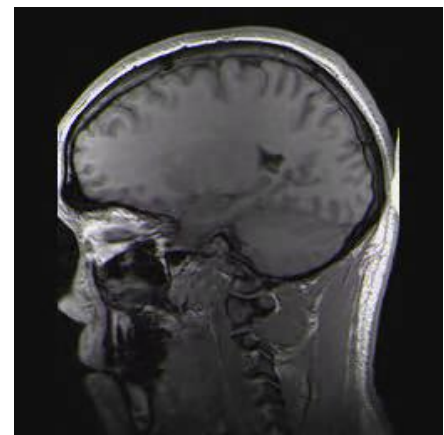
Magnetic resonance imaging is a relatively new technology. The first MR image was published in 1973^{[2] [3]} and the first cross-sectional



Sagittal MR image of the knee

image of a living mouse was published in January 1974.^[4] The first studies performed on humans were published in 1977.^[5] ^[6] By comparison, the first human X-ray image was taken in 1895.

Magnetic resonance imaging is a development of nuclear magnetic resonance. Originally, the technique was referred to as nuclear magnetic resonance imaging (NMRI). However, because the word *nuclear* was associated in the public mind with ionizing radiation exposure, it is generally now referred to simply as MRI. Scientists still use the term NMRI when discussing non-medical devices operating on the same principles. The term magnetic resonance tomography (MRT) is also sometimes used.



Para-sagittal MRI of the head, with aliasing artifacts (nose and forehead appear at the back of the head)

How MRI works

The body is largely composed of water molecules. Each water molecule has two hydrogen nuclei or protons. When a person goes inside the powerful magnetic field of the scanner, the magnetic moments of some of these protons changes, and aligns with the direction of the field.

Photons are the carriers of electromagnetic radiation such as light, and electromagnetism. All photons travel at the speed of light in a vacuum and therefore cannot carry differing amounts of energy due to their velocity. Their energy is manifested by frequency — higher energy, higher frequency.

In an MRI machine a radio frequency transmitter is briefly turned on, producing an electromagnetic field. The photons of this field have just the right energy, known as the resonance frequency, to flip the spin of the aligned protons in the body. As the intensity and duration of the field increases, more aligned spins are affected. After the field is turned off, the protons decay to the original spin-down state and the difference in energy between the two states is released as a photon. It is these photons that produce the electromagnetic signal that the scanner detects. The frequency the protons resonate at depends on the strength of the magnetic field. As a result of conservation of energy, this also dictates the frequency of the released photons. The photons released when the field is removed have an energy — and therefore a frequency — due to the amount of energy the protons absorbed while the field was active.

It is this relationship between field-strength and frequency that allows the use of nuclear magnetic resonance for imaging. Additional magnetic fields are applied during the scan to make the magnetic field strength depend on the position within the patient, providing a straightforward method to control where the protons are excited by the radio photons. These fields are created by passing electric currents through solenoids, known as gradient coils. Since these coils are within the bore of the scanner, there are large forces between them and the main field coils, producing most of the noise that is heard during operation. Without efforts to dampen this noise, it can approach 130 decibels (dB) with strong fields ^[7] (see also #Acoustic_noise).

An image can be constructed because the protons in different tissues return to their equilibrium state at different rates, which is a difference that can be detected. By changing the parameters on the scanner, this effect is used to create contrast between different types of body tissue or between other properties, as in fMRI and diffusion MRI.

Contrast agents may be injected intravenously to enhance the appearance of blood vessels, tumors or inflammation. Contrast agents may also be directly injected into a joint in the case of arthrograms, MRI images of joints. Unlike CT, MRI uses no ionizing radiation and is generally a very safe procedure. Nonetheless the strong magnetic fields

and radio pulses can affect metal implants, including cochlear implants and cardiac pacemakers. In the case of cardiac pacemakers, the results can sometimes be lethal,^[8] so patients with such implants are generally not eligible for MRI.

MRI is used to image every part of the body, and is particularly useful for tissues with many hydrogen nuclei and little density contrast, such as the brain, muscle, connective tissue and most tumors.

Applications

In clinical practice, MRI is used to distinguish pathologic tissue (such as a brain tumor) from normal tissue. One advantage of an MRI scan is that it is believed to be harmless to the patient. It uses strong magnetic fields and non-ionizing radiation in the radio frequency range, unlike CT scans and traditional X-rays, which both use ionizing radiation.

While CT provides good spatial resolution (the ability to distinguish two separate structures an arbitrarily small distance from each other), MRI provides comparable resolution with far better contrast resolution (the ability to distinguish the differences between two arbitrarily similar but not identical tissues). The basis of this ability is the complex library of *pulse sequences* that the modern medical MRI scanner includes, each of which is optimized to provide *image contrast* based on the chemical sensitivity of MRI.

For example, with particular values of the *echo time* (T_E) and the *repetition time* (T_R), which are basic parameters of image acquisition, a sequence takes on the property of T_2 -weighting. On a T_2 -weighted scan, water- and fluid-containing tissues are bright (most modern T_2 sequences are actually *fast* T_2 sequences) and fat-containing tissues are dark. The reverse is true for T_1 -weighted images. Damaged tissue tends to develop edema, which makes a T_2 -weighted sequence sensitive for pathology, and generally able to distinguish pathologic tissue from normal tissue. With the addition of an additional radio frequency pulse and additional manipulation of the magnetic gradients, a T_2 -weighted sequence can be converted to a **FLAIR** sequence, in which free water is now dark, but edematous tissues remain bright. This sequence in particular is currently the most sensitive way to evaluate the brain for demyelinating diseases, such as multiple sclerosis.

The typical MRI examination consists of 5–20 sequences, each of which are chosen to provide a particular type of information about the subject tissues. This information is then synthesized by the interpreting physician.

Basic MRI scans

T_1 -weighted MRI

T_1 -weighted scans use a gradient echo (GRE) sequence, with short T_E and short T_R . This is one of the basic types of MR contrast and is a commonly run clinical scan. The T_1 weighting can be increased (improving contrast) with the use of an inversion pulse as in an MP-RAGE sequence. Due to the short repetition time (T_R) this scan can be run very fast allowing the collection of high resolution 3D datasets. A T_1 reducing gadolinium contrast agent is also commonly used, with a T_1 scan being collected before and after administration of contrast agent to compare the difference. In the brain T_1 -weighted scans provide good gray matter/white matter contrast, in other words put SIMPLY, T1 Weighted Images highlights fat deposition.

T_2 -weighted MRI

T_2 -weighted scans use a spin echo (SE) sequence, with long T_E and long T_R . They have long been the clinical workhorse as the spin echo sequence is less susceptible to inhomogeneities in the magnetic field. They are particularly well suited to edema as they are sensitive to water content (edema is characterized by increased water content). In other words, put more simply, T2 weighted images light up liquid on the images being visualized.

T_2^* -weighted MRI

T_2^* (pronounced "T 2 star") weighted scans use a gradient echo (GRE) sequence, with long T_E and long T_R . The gradient echo sequence used does not have the extra refocusing pulse used in spin echo so it is subject to additional losses above the normal T_2 decay (referred to as T_2'), these taken together are called T_2^* . This also makes it more prone to susceptibility losses at air/tissue boundaries, but can increase contrast for certain types of tissue, such as venous blood.

Spin density weighted MRI

Spin density, also called proton density, weighted scans try to have no contrast from either T_2 or T_1 decay, the only signal change coming from differences in the amount of available spins (hydrogen nuclei in water). It uses a spin echo or sometimes a gradient echo sequence, with short T_E and long T_R .

Specialized MRI scans

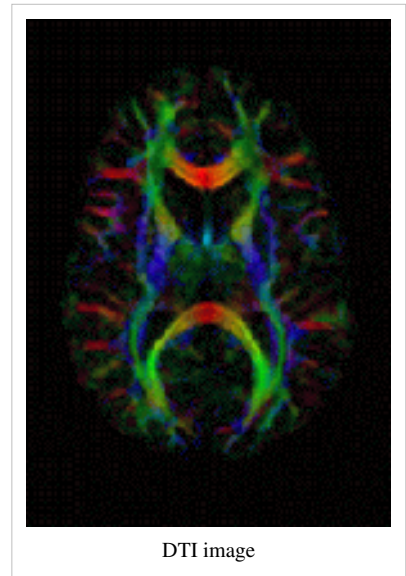
Diffusion MRI

Diffusion MRI measures the diffusion of water molecules in biological tissues.^[9] In an isotropic medium (inside a glass of water for example) water molecules naturally move randomly according to turbulence and Brownian motion. In biological tissues however, where the Reynold's number is low enough for flows to be laminar, the diffusion may be anisotropic. For example a molecule inside the axon of a neuron has a low probability of crossing the myelin membrane. Therefore the molecule moves principally along the axis of the neural fiber. If we know that molecules in a particular voxel diffuse principally in one direction we can make the assumption that the majority of the fibers in this area are going parallel to that direction.

The recent development of diffusion tensor imaging (DTI)^[3] enables diffusion to be measured in multiple directions and the fractional anisotropy in each direction to be calculated for each voxel. This enables researchers to make brain maps of fiber directions to examine the connectivity of different regions in the brain (using tractography) or to examine areas of neural degeneration and demyelination in diseases like Multiple Sclerosis.

Another application of diffusion MRI is diffusion-weighted imaging (DWI). Following an ischemic stroke, DWI is highly sensitive to the changes occurring in the lesion.^[10] It is speculated that increases in restriction (barriers) to water diffusion, as a result of cytotoxic edema (cellular swelling), is responsible for the increase in signal on a DWI scan. The DWI enhancement appears within 5–10 minutes of the onset of stroke symptoms (as compared with computed tomography, which often does not detect changes of acute infarct for up to 4–6 hours) and remains for up to two weeks. Coupled with imaging of cerebral perfusion, researchers can highlight regions of "perfusion/diffusion mismatch" that may indicate regions capable of salvage by reperfusion therapy.

Like many other specialized applications, this technique is usually coupled with a fast image acquisition sequence, such as echo planar imaging sequence.



Magnetization Transfer MRI

Magnetization transfer (MT) refers to the transfer of longitudinal magnetization from free water protons to hydration water protons in NMR and MRI.

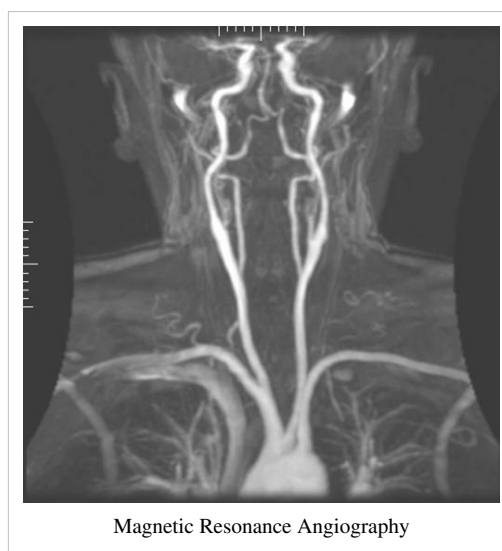
In magnetic resonance imaging of molecular solutions, such as protein solutions, two types of water molecules, free (bulk) and hydration (bound), are found. Free water protons have faster average rotational frequency and hence less fixed water molecules that may cause local field inhomogeneity. Because of this uniformity, most free water protons have resonance frequency lying narrowly around the normal proton resonance frequency of 63 MHz (at 1.5 teslas). This also results in slower transverse magnetization dephasing and hence longer T_2 . Conversely, hydration water molecules are slowed down by interaction with solute molecules and hence create field inhomogeneities that lead to wider resonance frequency spectrum.

Fluid attenuated inversion recovery (FLAIR)

Fluid Attenuated Inversion Recovery (FLAIR)^[11] is an inversion-recovery pulse sequence used to null signal from fluids. For example, it can be used in brain imaging to suppress cerebrospinal fluid (CSF) so as to bring out the periventricular hyperintense lesions, such as multiple sclerosis (MS) plaques. By carefully choosing the inversion time TI (the time between the inversion and excitation pulses), the signal from any particular tissue can be suppressed.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) generates pictures of the arteries to evaluate them for stenosis (abnormal narrowing) or aneurysms (vessel wall dilatations, at risk of rupture). MRA is often used to evaluate the arteries of the neck and brain, the thoracic and abdominal aorta, the renal arteries, and the legs (called a "run-off"). A variety of techniques can be used to generate the pictures, such as administration of a paramagnetic contrast agent (gadolinium) or using a technique known as "flow-related enhancement" (e.g. 2D and 3D time-of-flight sequences), where most of the signal on an image is due to blood that recently moved into that plane, see also FLASH MRI. Techniques involving phase accumulation (known as phase contrast angiography) can also be used to generate flow velocity maps easily and accurately. Magnetic resonance venography (MRV) is a similar procedure that is used to image veins. In this method, the tissue is now excited inferiorly, while signal is gathered in the plane immediately superior to the excitation plane—thus imaging the venous blood that recently moved from the excited plane.^[12]

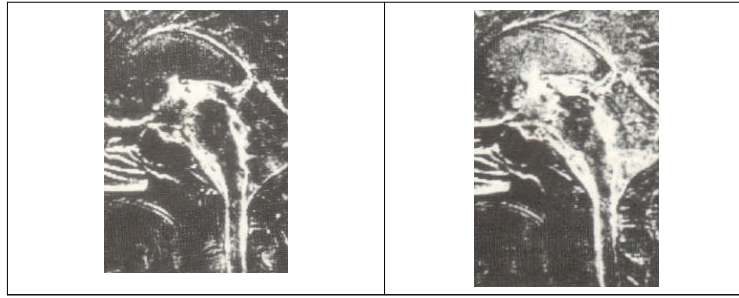


Magnetic Resonance Angiography

Magnetic resonance gated intracranial CSF dynamics (MR-GILD)

Magnetic resonance gated intracranial cerebrospinal fluid (CSF) or liquor dynamics (MR-GILD) technique is an MR sequence based on bipolar gradient pulse used to demonstrate CSF pulsatile flow in ventricles, cisterns, aqueduct of Sylvius and entire intracranial CSF pathway. It is a method for analyzing CSF circulatory system dynamics in patients with CSF obstructive lesions such as normal pressure hydrocephalus. It also allows visualization of both arterial and venous pulsatile blood flow in vessels without use of contrast agents.^{[13] [14]}

Diastolic time data acquisition (DTDA).	Systolic time data acquisition (STDA).
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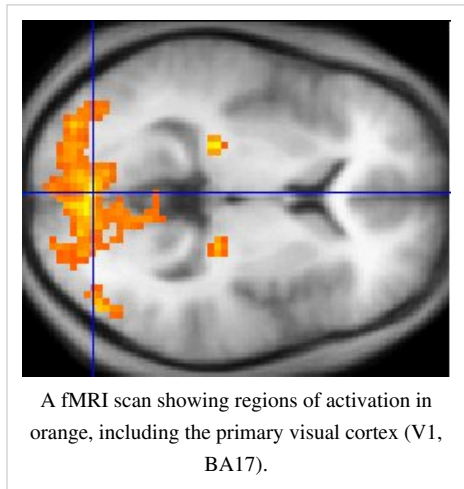
Magnetic resonance spectroscopy

Magnetic resonance spectroscopy (MRS) is used to measure the levels of different metabolites in body tissues. The MR signal produces a spectrum of resonances that correspond to different molecular arrangements of the isotope being "excited". This signature is used to diagnose certain metabolic disorders, especially those affecting the brain,^[15] and to provide information on tumor metabolism.^[16]

Magnetic resonance spectroscopic imaging (MRSI) combines both spectroscopic and imaging methods to produce spatially localized spectra from within the sample or patient. The spatial resolution is much lower (limited by the available SNR), but the spectra in each voxel contains information about many metabolites. Because the available signal is used to encode spatial and spectral information, MRSI requires high SNR achievable only at higher field strengths (3 T and above).

Functional MRI

Functional MRI (fMRI) measures signal changes in the brain that are due to changing neural activity. The brain is scanned at low resolution but at a rapid rate (typically once every 2–3 seconds). Increases in neural activity cause changes in the MR signal via T_2^* changes;^[17] this mechanism is referred to as the BOLD (blood-oxygen-level dependent) effect. Increased neural activity causes an increased demand for oxygen, and the vascular system actually overcompensates for this, increasing the amount of oxygenated hemoglobin relative to deoxygenated hemoglobin. Because deoxygenated hemoglobin attenuates the MR signal, the vascular response leads to a signal increase that is related to the neural activity. The precise nature of the relationship between neural activity and the BOLD signal is a subject of current research. The BOLD effect also allows for the generation of high resolution 3D maps of the venous vasculature within neural tissue.



While BOLD signal is the most common method employed for neuroscience studies in human subjects, the flexible nature of MR imaging provides means to sensitize the signal to other aspects of the blood supply. Alternative techniques employ arterial spin labeling (ASL) or weight the MRI signal by cerebral blood flow (CBF) and cerebral blood volume (CBV). The CBV method requires injection of a class of MRI contrast agents that are now in human clinical trials. Because this method has been shown to be far more sensitive than the BOLD technique in preclinical studies, it may potentially expand the role of fMRI in clinical applications. The CBF method provides more quantitative information than the BOLD signal, albeit at a significant loss of detection sensitivity.

Interventional MRI

The lack of harmful effects on the patient and the operator make MRI well-suited for "interventional radiology", where the images produced by a MRI scanner are used to guide minimally invasive procedures. Of course, such procedures must be done without *any* ferromagnetic instruments.

A specialized growing subset of interventional MRI is that of intraoperative MRI in which the MRI is used in the surgical process. Some specialized MRI systems have been developed that allow imaging concurrent with the surgical procedure. More typical, however, is that the surgical procedure is temporarily interrupted so that MR images can be acquired to verify the success of the procedure or guide subsequent surgical work.

Radiation therapy simulation

Because of MRI's superior imaging of soft tissues, it is now being utilized to specifically locate tumors within the body in preparation for radiation therapy treatments. For therapy simulation, a patient is placed in specific, reproducible, body position and scanned. The MRI system then computes the precise location, shape and orientation of the tumor mass, correcting for any spatial distortion inherent in the system. The patient is then marked or tattooed with points that, when combined with the specific body position, permits precise triangulation for radiation therapy.

Current density imaging

Current density imaging (CDI) endeavors to use the phase information from images to reconstruct current densities within a subject. Current density imaging works because electrical currents generate magnetic fields, which in turn affect the phase of the magnetic dipoles during an imaging sequence. To date no successful CDI has been performed using biological currents, but several studies have been published that involve currents applied through a pair of electrodes.

Magnetic resonance guided focused ultrasound

In MRgFUS therapy, ultrasound beams are focused on a tissue—guided and controlled using MR thermal imaging—and due to the significant energy deposition at the focus, temperature within the tissue rises to more than 65 °C (150 °F), completely destroying it. This technology can achieve precise "ablation" of diseased tissue. MR imaging provides a three-dimensional view of the target tissue, allowing for precise focusing of ultrasound energy. The MR imaging provides quantitative, real-time, thermal images of the treated area. This allows the physician to ensure that the temperature generated during each cycle of ultrasound energy is sufficient to cause thermal ablation within the desired tissue and if not, to adapt the parameters to ensure effective treatment.

Multinuclear imaging

Hydrogen is the most frequently imaged nucleus in MRI because it is present in biological tissues in great abundance. However, any nucleus with a net nuclear spin could potentially be imaged with MRI. Such nuclei include helium-3, carbon-13, fluorine-19, oxygen-17, sodium-23, phosphorus-31 and xenon-129. ^{23}Na , ^{31}P and ^{17}O are naturally abundant in the body, so can be imaged directly. Gaseous isotopes such as ^3He or ^{129}Xe must be hyperpolarized and then inhaled as their nuclear density is too low to yield a useful signal under normal conditions. ^{17}O , ^{13}C and ^{19}F can be administered in sufficient quantities in liquid form (e.g. ^{17}O -water, ^{13}C -glucose solutions or perfluorocarbons) that hyperpolarization is not a necessity.

Multinuclear imaging is primarily a research technique at present. However, potential applications include functional imaging and imaging of organs poorly seen on ^1H MRI (e.g. lungs and bones) or as alternative contrast agents. Inhaled hyperpolarized ^3He can be used to image the distribution of air spaces within the lungs. Injectable solutions containing ^{13}C or stabilized bubbles of hyperpolarized ^{129}Xe have been studied as contrast agents for angiography and perfusion imaging. ^{31}P can potentially provide information on bone density and structure, as well as functional imaging of the brain.

Susceptibility weighted imaging (SWI)

Susceptibility weighted imaging (SWI), is a new type of contrast in MRI different from spin density, T_1 , or T_2 imaging. This method exploits the susceptibility differences between tissues and uses a fully velocity compensated, three dimensional, RF spoiled, high-resolution, 3D gradient echo scan. This special data acquisition and image processing produces an enhanced contrast magnitude image very sensitive to venous blood, hemorrhage and iron storage. It is used to enhance the detection and diagnosis of tumors, vascular and neurovascular diseases (stroke and hemorrhage, multiple sclerosis, Alzheimer's), and also detects traumatic brain injuries that may not be diagnosed using other methods"Radiology"^[18]. Retrieved 2 August 2010. (subscription required)</ref></ref>

Other specialized MRI techniques

MRI is a new and active field of research and new methods and variants are often published when they are able to get better results in specific fields. Examples of these recent improvements are T_2^* -weighted turbo spin-echo (T_2 TSE MRI), double inversion recovery MRI (DIR-MRI) or phase-sensitive inversion recovery MRI (PSIR-MRI), all of them able to improve imaging of the brain lesions.^{[19] [20]} Another example is MP-RAGE (magnetization-prepared rapid acquisition with gradient echo),^[21] which improves images of multiple sclerosis cortical lesions.^[22]

Portable instruments

Portable magnetic resonance instruments are available for use in education and field research. Using the principles of Earth's field NMR, they have no powerful polarizing magnet, so that such instruments can be small and inexpensive. Some can be used for both EFNMR spectroscopy and MRI imaging.^[23] The low strength of the Earth's field results in poor signal to noise ratios, requiring long scan times to capture spectroscopic data or build up MRI images.

Research with atomic magnetometers have discussed the possibility for cheap and portable MRI instruments without the large magnet.^{[24] [25]}

MRI versus CT

A computed tomography (CT) scanner uses X-rays, a type of ionizing radiation, to acquire its images, making it a good tool for examining tissue composed of elements of a higher atomic number than the tissue surrounding them, such as bone and calcifications (calcium based) within the body (carbon based flesh), or of structures (vessels, bowel). MRI, on the other hand, uses non-ionizing radio frequency (RF) signals to acquire its images and is best suited for non-calcified tissue, though MR images can also be acquired from bones and teeth^[26] as well as fossils.^[27]

CT may be enhanced by use of contrast agents containing elements of a higher atomic number than the surrounding flesh such as iodine or barium. Contrast agents for MRI have paramagnetic properties, e.g., gadolinium and manganese.

Both CT and MRI scanners are able to generate multiple two-dimensional cross-sections (slices) of tissue and three-dimensional reconstructions. Unlike CT, which uses only X-ray attenuation to generate image contrast, MRI has a long list of properties that may be used to generate image contrast. By variation of scanning parameters, tissue contrast can be altered and enhanced in various ways to detect different features. (See Applications above.)

MRI can generate cross-sectional images in any plane (including oblique planes). In the past, CT was limited to acquiring images in the axial (or near axial) plane. The scans used to be called Computed *Axial* Tomography scans (CAT scans). However, the development of multi-detector CT scanners with near-isotropic resolution, allows the CT scanner to produce data that can be retrospectively reconstructed in any plane with minimal loss of image quality.

For purposes of tumor detection and identification in the brain, MRI is generally superior.^{[28] [29] [30]} However, in the case of solid tumors of the abdomen and chest, CT is often preferred due to less motion artifact. Furthermore, CT usually is more widely available, faster, less expensive, and may be less likely to require the person to be sedated or anesthetized.

MRI is also best suited for cases when a patient is to undergo the exam several times successively in the short term, because, unlike CT, it does not expose the patient to the hazards of ionizing radiation.

Economics of MRI

MRI equipment is expensive. 1.5 tesla scanners often cost between \$1 million and \$1.5 million USD. 3.0 tesla scanners often cost between \$2 million and \$2.3 million USD. Construction of MRI suites can cost up to \$500,000 USD, or more, depending on project scope.

MRI scanners have been significant sources of revenue for healthcare providers in the US. This is because of favorable reimbursement rates from insurers and federal government programs. Insurance reimbursement is provided in two components, an equipment charge for the actual performance of the MRI scan and professional charge for the radiologist's review of the images and/or data. In the US Northeast, an equipment charge might be \$3,500 and a professional charge might be \$350^[31] although the actual fees received by the equipment owner and interpreting physician are often significantly less and depend on the rates negotiated with insurance companies or determined by governmental action as in the Medicare Fee Schedule. For example, an orthopedic surgery group in Illinois billed a charge of \$1,116 for a knee MRI in 2007 but the Medicare reimbursement in 2007 was only \$470.91.^[32] Many insurance companies require preapproval of an MRI procedure as a condition for coverage.

In the US, the 2007 Deficit Reduction Act (DRA) significantly reduced reimbursement rates paid by federal insurance programs for the equipment component of many scans, shifting the economic landscape. Many private insurers have followed suit.



Looking through an MRI scanner.

Installation of the MRI unit



Heavy lifting equipment is used to install the MRI unit.

An MRI unit is a rather large item, typically requiring heavy equipment (such as cranes) to move the unit to its final location. Once the MRI unit is in place, the room that houses it is usually "built up" around the unit itself. See this page^[33] for an example of the complexity involved in installing an MRI unit in a clinical setting.^[34]

Safety

Death and injuries have occurred from projectiles created by the magnetic field, although few compared to the millions of examinations administered.^[35]^[36] MRI makes use of powerful magnetic fields that, though not known to cause direct biological damage, can interfere with metallic and electromechanical devices. Additional (small) risks are presented by the radio frequency systems, components or elements of the MRI system's operation, elements of the scanning procedure and medications that may be administered to facilitate MRI imaging.

Of great concern is the dramatic increase in the number of reported MRI accidents to the U.S. Food and Drug Administration (FDA). Since 2004, the last year in which a decline in the number of MRI accidents was reported, the full spectrum of MRI accidents has increased significantly in the following years. The 2008 FDA accident report data^[37] culminates in a 277% increase over the 2004 rate.

There are many steps that the MRI patient and referring physician can take to help reduce the remaining risks, including providing a full, accurate and thorough medical history to the MRI provider.

Several of the specific MRI safety considerations are identified below:

Implants and foreign bodies

Pacemakers are generally considered an absolute contraindication towards MRI scanning, though highly specialized protocols have been developed to permit scanning of select pacing devices. Several cases of arrhythmia or death have been reported in patients with pacemakers who have undergone MRI scanning without appropriate precautions. Other electronic implants have varying contraindications, depending upon scanner technology, and implant properties, scanning protocols and anatomy being imaged.

Many other forms of medical or biostimulation implants may be contraindicated for MRI scans. These may include vagus nerve stimulators, implantable cardioverter-defibrillators, loop recorders, insulin pumps, cochlear implants, deep brain stimulators, and many others. Medical device patients should always present complete information (manufacturer, model, serial number and date of implantation) about all implants to both the referring physician and to the radiologist or technologist before entering the room for the MRI scan.

While these implants pose a current problem, scientists and manufacturers are working on improved designs that reduce risks to medical device operations. One such development in the works is a nano-coating for implants intended to screen them from the radio frequency waves, helping to make MRI exams available to patients currently prohibited from receiving them. The current article^[38] for this is from New Scientist.

Ferromagnetic foreign bodies (e.g. shell fragments), or metallic implants (e.g. surgical prostheses, aneurysm clips) are also potential risks, and safety aspects need to be considered on an individual basis. Interaction of the magnetic and radio frequency fields with such objects can lead to trauma due to movement of the object in the magnetic field, thermal injury from radio-frequency induction heating of the object, or failure of an implanted device. These issues are especially problematic when dealing with the eye. Most MRI centers require an orbital x-ray to be performed on anyone suspected of having metal fragments in their eyes, something not uncommon in metalworking.

Because of its non-ferromagnetic nature and poor electrical conductivity, titanium and its alloys are useful for long term implants and surgical instruments intended for use in image-guided surgery. In particular, not only is titanium safe from movement from the magnetic field, but artifacts around the implant are less frequent and less severe than with more ferromagnetic materials e.g. stainless steel. Artifacts from metal frequently appear as regions of empty space around the implant—frequently called 'black-hole artifact'. E.g. a 3 mm titanium alloy coronary stent may appear as a 5 mm diameter region of empty space on MRI, whereas around a stainless steel stent, the artifact may extend for 10–20 mm or more.

In 2006, a new classification system for implants and ancillary clinical devices has been developed by ASTM International and is now the standard supported by the US Food and Drug Administration:

MR-Safe — The device or implant is completely non-magnetic, non-electrically conductive, and non-RF reactive, eliminating all of the primary potential threats during an MRI procedure.



MR Safe sign

MR-Conditional — A device or implant that may contain magnetic, electrically conductive or RF-reactive components that is safe for operations in proximity to the MRI, provided the conditions for safe operation are defined and observed (such as 'tested safe to 1.5 teslas' or 'safe in magnetic fields below 500 gauss in strength').



MR Conditional sign

MR-Unsafe — Nearly self-explanatory, this category is reserved for objects that are significantly ferromagnetic and pose a clear and direct threat to persons and equipment within the magnet room.

Though the current classification system was originally developed for regulatory-approved medical devices, it is being applied to all manner of items, appliances and equipment intended for use in the MR environment.

In the case of pacemakers, the risk is thought to be primarily RF induction in the pacing electrodes/wires causing inappropriate pacing of the heart, rather than the magnetic field affecting the pacemaker itself. Much research and development is being undertaken, and many tools are being developed to predict RF field effects inside the body.



MR Unsafe sign

Projectile or missile effect

As a result of the very high strength of the magnetic field needed to produce scans (frequently up to 60,000 times the Earth's own magnetic field effects), there are several incidental safety issues addressed in MRI facilities. Missile-effect accidents, where ferromagnetic objects are attracted to the center of the magnet, have resulted in injury and death.^{[35] [36]}

To reduce the risks of projectile accidents, ferromagnetic objects and devices are typically prohibited in proximity to the MRI scanner, with non-ferromagnetic versions of many tools and devices typically retained by the scanning facility. Patients undergoing MRI examinations are required to remove all metallic objects, often by changing into a gown or scrubs.

Ferromagnetic detection devices are used by some sites as a supplement conventional screening techniques, and are now recommended by the American College of Radiology's *Guidance Document for Safe MR Practices*^[39] and the United States Department of Veterans Affairs^[40].

The magnetic field and the associated risk of missile-effect accidents remains a permanent hazard, as superconductive MRI magnets are kept permanently energized and so retain their magnetic field in the event of a power outage.

Radio frequency energy

A powerful radio transmitter is needed for excitation of proton spins. This can heat the body to the point of risk of hyperthermia in patients, particularly in obese patients or those with thermoregulation disorders. Several countries have issued restrictions on the maximum specific absorption rate that a scanner may produce.

Peripheral nerve stimulation (PNS)

The rapid switching on and off of the magnetic field gradients is capable of causing nerve stimulation. Volunteers report a twitching sensation when exposed to rapidly switched fields, particularly in their extremities. The reason the peripheral nerves are stimulated is that the changing field increases with distance from the center of the gradient coils (which more or less coincides with the center of the magnet). Note however that when imaging the head, the heart is far off-center and induction of even a tiny current into the heart must be avoided at all costs. Although PNS was not a problem for the slow, weak gradients used in the early days of MRI, the strong, rapidly switched gradients used in techniques such as EPI, fMRI, diffusion MRI, etc. are indeed capable of inducing PNS. American and European regulatory agencies insist that manufacturers stay below specified dB/dt limits (dB/dt is the change in field per unit time) or else prove that no PNS is induced for any imaging sequence. As a result of dB/dt limitation, commercial MRI systems cannot use the full rated power of their gradient amplifiers.

Acoustic noise

Switching of field gradients causes a change in the Lorentz force experienced by the gradient coils, producing minute expansions and contractions of the coil itself. As the switching is typically in the audible frequency range, the resulting vibration produces loud noises (clicking or beeping). This is most marked with high-field machines and rapid-imaging techniques in which sound intensity can reach 120 dB(A) (equivalent to a jet engine at take-off).^[41] As a reference, 120 dB is the threshold of loudness causing sensation in the human ear canal — tickling, and 140 dB is the threshold of ear pain. Since decibel is a logarithmic measurement, a 10 dB increase equates to a 10-fold increase in intensity—which, in acoustics, is roughly equal to a doubling of loudness.

Appropriate use of ear protection is essential for anyone inside the MRI scanner room during the examination.^[42]

Cryogenics

As described above in #Scanner construction and operation, many MRI scanners rely on cryogenic liquids to enable superconducting capabilities of the electromagnetic coils within. Though the cryogenic liquids used are non-toxic, their physical properties present specific hazards.

An unintentional shut-down of a superconducting electromagnet, an event known as "quench", involves the rapid boiling of liquid helium from the device. If the rapidly expanding helium cannot be dissipated through an external vent, sometimes referred to as 'quench pipe', it may be released into the scanner room where it may cause displacement of the oxygen and present a risk of asphyxiation.^[43]

Liquid helium, the most commonly used cryogen in MRI, undergoes near explosive expansion as it changes from liquid to a gaseous state. Rooms built in support of superconducting MRI equipment should be equipped with pressure relief mechanisms^[44] and an exhaust fan, in addition to the required quench pipe.

Since a quench results in rapid loss of all cryogenics in the magnet, recommissioning the magnet is expensive and time-consuming. Spontaneous quenches are uncommon, but may also be triggered by equipment malfunction, improper cryogen fill technique, contaminants inside the cryostat, or extreme magnetic or vibrational disturbances.

Contrast agents

The most commonly used intravenous contrast agents are based on chelates of gadolinium. In general, these agents have proved safer than the iodinated contrast agents used in X-ray radiography or CT. Anaphylactoid reactions are rare, occurring in approx. 0.03–0.1%.^[45] Of particular interest is the lower incidence of nephrotoxicity, compared with iodinated agents, when given at usual doses—this has made contrast-enhanced MRI scanning an option for patients with renal impairment, who would otherwise not be able to undergo contrast-enhanced CT.^[46]

Although gadolinium agents have proved useful for patients with renal impairment, in patients with severe renal failure requiring dialysis there is a risk of a rare but serious illness, nephrogenic systemic fibrosis, that may be linked to the use of certain gadolinium-containing agents. The most frequently linked is gadodiamide, but other agents have been linked too.^[47] Although a causal link has not been definitively established, current guidelines in the United States are that dialysis patients should only receive gadolinium agents where essential, and that dialysis should be performed as soon as possible after the scan to remove the agent from the body promptly.^[48] In Europe, where more gadolinium-containing agents are available, a classification of agents according to potential risks has been released.^[49] ^[50] Recently a new contrast agent named gadoxetate, brand name Eovist (US) or Primovist (EU), was approved for diagnostic use: this has the theoretical benefit of a dual excretion path.^[51]

Pregnancy

No effects of MRI on the fetus have been demonstrated.^[52] In particular, MRI avoids the use of ionizing radiation, to which the fetus is particularly sensitive. However, as a precaution, current guidelines recommend that pregnant women undergo MRI only when essential. This is particularly the case during the first trimester of pregnancy, as organogenesis takes place during this period. The concerns in pregnancy are the same as for MRI in general, but the fetus may be more sensitive to the effects—particularly to heating and to noise. However, one additional concern is the use of contrast agents; gadolinium compounds are known to cross the placenta and enter the fetal bloodstream, and it is recommended that their use be avoided.

Despite these concerns, MRI is rapidly growing in importance as a way of diagnosing and monitoring congenital defects of the fetus because it can provide more diagnostic information than ultrasound and it lacks the ionizing radiation of CT. MRI without contrast agents is the imaging mode of choice for pre-surgical, in-utero diagnosis and evaluation of fetal tumors, primarily teratomas, facilitating open fetal surgery, other fetal interventions, and planning for procedures (such as the EXIT procedure) to safely deliver and treat babies whose defects would otherwise be fatal.

Claustrophobia and discomfort

Due to the construction of some MRI scanners, they can be potentially unpleasant to lie in. Older models of closed bore MRI systems feature a fairly long tube or tunnel. The part of the body being imaged must lie at the center of the magnet, which is at the absolute center of the tunnel. Because scan times on these older scanners may be long (occasionally up to 40 minutes for the entire procedure), people with even mild claustrophobia are sometimes unable to tolerate an MRI scan without management. Modern scanners may have larger bores (up to 70 cm) and scan times are shorter. This means that claustrophobia is less of an issue, and many patients now find MRI an innocuous and easily tolerated procedure.

Nervous patients may still find the following strategies helpful:

- Advance preparation
 - visiting the scanner to see the room and practice lying on the table
 - visualization techniques
 - chemical sedation
 - general anesthesia
- Coping while inside the scanner
 - holding a "panic button"
 - closing eyes as well as covering them (e.g. washcloth, eye mask)
 - listening to music on headphones or watching a movie with a Head-mounted display while in the machine

Alternative scanner designs, such as open or upright systems, can also be helpful where these are available. Though open scanners have increased in popularity, they produce inferior scan quality because they operate at lower magnetic fields than closed scanners. However, commercial 1.5 tesla open systems have recently become available, providing much better image quality than previous lower field strength open models.^[53]

For babies and young children chemical sedation or general anesthesia are the norm, as these subjects cannot be instructed to hold still during the scanning session. Obese patients and pregnant women may find the MRI machine to be a tight fit. Pregnant women may also have difficulty lying on their backs for an hour or more without moving.

Guidance

Safety issues, including the potential for biostimulation device interference, movement of ferromagnetic bodies, and incidental localized heating, have been addressed in the American College of Radiology's *White Paper on MR Safety*, which was originally published in 2002 and expanded in 2004. The *ACR White Paper on MR Safety* has been rewritten and was released early in 2007 under the new title *ACR Guidance Document for Safe MR Practices*^[54].

In December 2007, the Medicines in Healthcare product Regulation Agency (MHRA), a UK healthcare regulatory body, issued their *Safety Guidelines for Magnetic Resonance Imaging Equipment in Clinical Use*^[55].

In February 2008, the Joint Commission, a US healthcare accrediting organization, issued a Sentinel Event Alert #38^[56], their highest patient safety advisory, on MRI safety issues.

In July 2008, the United States Veterans Administration, a federal governmental agency serving the healthcare needs of former military personnel, issued a substantial revision to their *MRI Design Guide*^[57], which includes physical or facility safety considerations.

The European Physical Agents Directive

The European Physical Agents (Electromagnetic Fields) Directive is legislation adopted in European legislature. Originally scheduled to be required by the end of 2008, each individual state within the European Union must include this directive in its own law by the end of 2012. Some member nations passed complying legislation and are now attempting to repeal their state laws in expectation that the final version of the EU Physical Agents Directive will be substantially revised prior to the revised adoption date.

The directive applies to occupational exposure to electromagnetic fields (not medical exposure) and was intended to limit workers' acute exposure to strong electromagnetic fields, as may be found near electricity substations, radio or television transmitters or industrial equipment. However, the regulations impact significantly on MRI, with separate sections of the regulations limiting exposure to static magnetic fields, changing magnetic fields and radio frequency energy. Field strength limits are given, which may not be exceeded. An employer may commit a criminal offense by allowing a worker to exceed an exposure limit, if that is how the Directive is implemented in a particular member state.

The Directive is based on the international consensus of established effects of exposure to electromagnetic fields, and in particular the advice of the European Commissions's advisor, the International Commission on Non-Ionizing Radiation Protection (ICNIRP). The aims of the Directive, and the ICNIRP guidelines it is based on, are to prevent exposure to potentially harmful fields. The actual limits in the Directive are very similar to the limits advised by the Institute of Electrical and Electronics Engineers, with the exception of the frequencies produced by the gradient coils, where the IEEE limits are significantly higher.

Many Member States of the EU already have either specific EMF regulations or (as in the UK) a general requirement under workplace health and safety legislation to protect workers against electromagnetic fields. In almost all cases the existing regulations are aligned with the ICNIRP limits so that the Directive should, in theory, have little impact on any employer already meeting their legal responsibilities.

The introduction of the Directive has brought to light an existing potential issue with occupational exposures to MRI fields. There are at present very few data on the number or types of MRI practice that might lead to exposures in excess of the levels of the Directive.^{[58] [59]} There is a justifiable concern amongst MRI practitioners that if the Directive were to be enforced more vigorously than existing legislation, the use of MRI might be restricted, or working practices of MRI personnel might have to change.

In the initial draft a limit of static field strength to 2 T was given. This has since been removed from the regulations, and whilst it is unlikely to be restored as it was without a strong justification, some restriction on static fields may be reintroduced after the matter has been considered more fully by ICNIRP. The effect of such a limit might be to restrict the installation, operation and maintenance of MRI scanners with magnets of 2 T and stronger. As the increase in field strength has been instrumental in developing higher resolution and higher performance scanners, this would be a significant step back. This is why it is unlikely to happen without strong justification.

Individual government agencies and the European Commission have now formed a working group to examine the implications on MRI and to try to address the issue of occupational exposures to electromagnetic fields from MRI.

Three-dimensional (3D) image reconstruction

The principle

Because contemporary MRI scanners offer isotropic, or near isotropic, resolution, display of images does not need to be restricted to the conventional axial images. Instead, it is possible for a software program to build a volume by 'stacking' the individual slices one on top of the other. The program may then display the volume in an alternative manner.

3D rendering techniques

Surface rendering

A threshold value of greyscale density is chosen by the operator (e.g. a level that corresponds to fat). A threshold level is set, using edge detection image processing algorithms. From this, a 3-dimensional model can be constructed and displayed on screen. Multiple models can be constructed from various different thresholds, allowing different colors to represent each anatomical component such as bone, muscle, and cartilage.

However, the interior structure of each element is not visible in this mode of operation.

Volume rendering

Surface rendering is limited in that it only displays surfaces that meet a threshold density, and only displays the surface closest to the imaginary viewer. In volume rendering, transparency and colors are used to allow a better representation of the volume to be shown in a single image - e.g. the bones of the pelvis could be displayed as semi-transparent, so that even at an oblique angle, one part of the image does not conceal another.

Image segmentation

Where different structures have similar threshold density, it can become impossible to separate them simply by adjusting volume rendering parameters. The solution is called segmentation, a manual or automatic procedure that can remove the unwanted structures from the image.

2003 Nobel Prize

Reflecting the fundamental importance and applicability of MRI in medicine, Paul Lauterbur of the University of Illinois at Urbana-Champaign and Sir Peter Mansfield of the University of Nottingham were awarded the 2003 Nobel Prize in Physiology or Medicine for their "discoveries concerning magnetic resonance imaging". The Nobel citation acknowledged Lauterbur's insight of using magnetic field gradients to determine spatial localization, a discovery that allowed rapid acquisition of 2D images. Mansfield was credited with introducing the mathematical formalism and developing techniques for efficient gradient utilization and fast imaging. The actual research that won the prize was done almost 30 years before, while Paul Lauterbur was at Stony Brook University in New York.

The award was vigorously protested by Raymond Vahan Damadian, founder of FONAR Corporation, who claimed that he invented the MRI,^[3] and that Lauterbur and Mansfield had merely refined the technology.^[60] An ad hoc group, called "The Friends of Raymond Damadian", took out full-page advertisements in the *New York Times* and *The Washington Post* entitled "The Shameful Wrong That Must Be Righted", demanding that he be awarded at least a share of the Nobel Prize.^[61] Also, even earlier, in the Soviet Union, Vladislav Ivanov filed (in 1960) a document with the USSR State Committee for Inventions and Discovery at Leningrad for a Magnetic Resonance Imaging device,^[62] although this was not approved until the 1970s.^[63] In a letter to *Physics Today*, Herman Carr pointed out his own even earlier use of field gradients for one-dimensional MR imaging.^[64]

See also

- Earth's field NMR (EFNMR)
- Electron-spin resonance (spin physics)
- History of brain imaging
- Medical imaging
- Magnetic immunoassay
- Jemris (open source MRI simulator)
- *Magnetic Resonance Imaging (journal)*
- Magnetic resonance microscopy
- Magnetic Particle Imaging (MPI)
- Magnetic resonance elastography
- Neuroimaging software
- Nephrogenic fibrosing dermopathy
- Nobel Prize controversies
- Nuclear magnetic resonance (NMR)
- 2D-FT NMRI and Spectroscopy
- Relaxation
- Robinson oscillator
- Rabi cycle
- Virtopsy

Further reading

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External links

- A Guided Tour of MRI: An introduction for laypeople^[65] National High Magnetic Field Laboratory
- The Basics of MRI^[66]. *Underlying physics and technical aspects*.
- Video: What to Expect During Your MRI Exam^[67] from the Institute for Magnetic Resonance Safety, Education, and Research (IMRSER)
- International Society for Magnetic Resonance in Medicine^[68]
- Trends in Biotechnology Volume 28, Issue 7, July 2010, Pages 363-370^[69]

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ESR Spectroscopy and Microspectroscopy

ESR

Electron paramagnetic resonance (EPR) or **electron spin resonance (ESR)** spectroscopy is a technique for studying chemical species that have one or more unpaired electrons, such as organic and inorganic free radicals or inorganic complexes possessing a transition metal ion. The basic physical concepts of EPR are analogous to those of nuclear magnetic resonance (NMR), but it is electron spins that are excited instead of spins of atomic nuclei. Because most stable molecules have all their electrons paired, the EPR technique is less widely used than NMR. However, this limitation to paramagnetic species also means that the EPR technique is one of great specificity, since ordinary chemical solvents and matrices do not give rise to EPR spectra.

EPR was first observed in Kazan State University by Soviet physicist Yevgeny Zavoisky in 1944, and was developed independently at the same time by Brebis Bleaney at Oxford University.

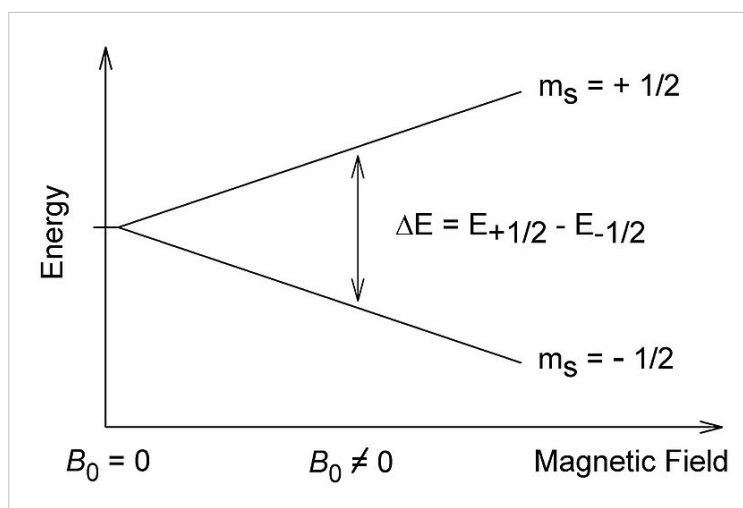
Theory

Origin of an EPR signal

Every electron has a magnetic moment and spin quantum number $s = 1/2$, with magnetic components $m_s = +1/2$ and $m_s = -1/2$. In the presence of an external magnetic field with strength B_0 , the electron's magnetic moment aligns itself either parallel ($m_s = -1/2$) or antiparallel ($m_s = +1/2$) to the field, each alignment having a specific energy (see the Zeeman effect). The parallel alignment corresponds to the lower energy state, and the separation between it and the upper state is $\Delta E = g_e \mu_B B_0$, where g_e is the electron's so-called g -factor (see also the Landé g -factor) and μ_B is the Bohr magneton. This equation implies that the splitting of the energy levels is directly proportional to the magnetic field's strength, as shown in the diagram below.



EPR spectrometer



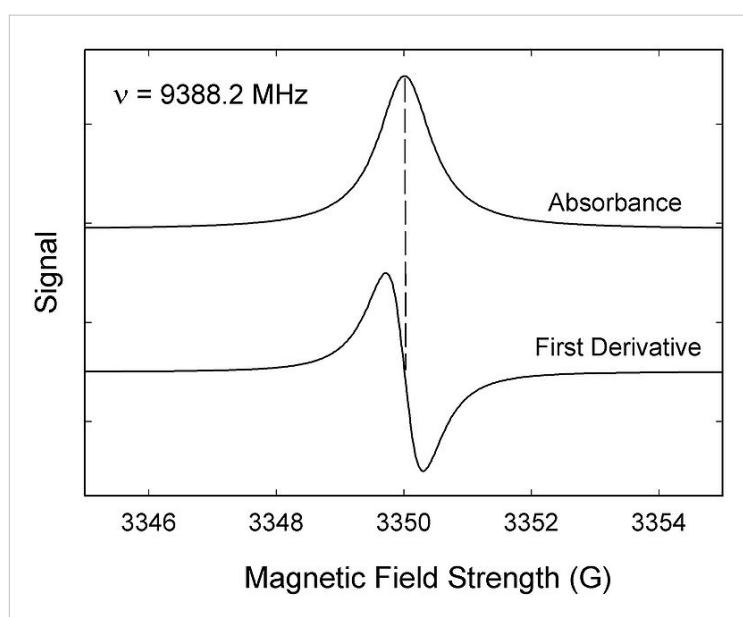
An unpaired electron can move between the two energy levels by either absorbing or emitting electromagnetic radiation of energy $\epsilon = h\nu$ such that the resonance condition, $\epsilon = \Delta E$, is obeyed. Substituting in $\epsilon = h\nu$ and $\Delta E = g\mu_B B_0$ leads to the fundamental equation of EPR spectroscopy: $h\nu = g\mu_B B_0$. Experimentally, this equation permits a large combination of frequency and magnetic field values, but the great majority of EPR measurements are made with microwaves in the 9000 – 10000 MHz (9 – 10 GHz) region, with fields corresponding to about 3500 G (0.35 T). See below for other field-frequency combinations.

In principle, EPR spectra can be generated by either varying the photon frequency incident on a sample while holding the magnetic field constant, or doing the reverse. In practice, it is usually the frequency which is kept fixed. A collection of paramagnetic centers, such as free radicals, is exposed to microwaves at a fixed frequency. By increasing an external magnetic field, the gap between the $m_s = +1/2$ and $m_s = -1/2$ energy states is widened until it matches the energy of the microwaves, as represented by the double-arrow in the diagram above. At this point the unpaired electrons can move between their two spin states. Since there typically are more electrons in the lower state, due to the Maxwell-Boltzmann distribution (see below), there is a net absorption of energy, and it is this absorption which is monitored and converted into a spectrum.

As an example of how $h\nu = g\mu_B B_0$ can be used, consider the case of a free electron, which has $g_e = 2.0023$,^[1] and the simulated spectrum shown at the right in two different forms. For the microwave frequency of 9388.2 MHz, the predicted resonance position is a magnetic field of about $B_0 = h\nu / g_e\mu_B = 0.3350$ tesla = 3350 gauss, as shown. Note that while two forms of the same spectrum are presented in the figure, most EPR spectra are recorded and published only as first derivatives.

Because of electron-nuclear mass differences, the magnetic moment of an electron is substantially larger than the corresponding quantity for any nucleus, so

that a much higher electromagnetic frequency is needed to bring about a spin resonance with an electron than with a nucleus, at identical magnetic field strengths. For example, for the field of 3350 G shown at the right, spin resonance occurs near 9388.2 MHz for an electron compared to only about 14.3 MHz for ^1H nuclei. (For NMR spectroscopy,



the corresponding resonance equation is $h\nu = g_N \mu_N B_0$ where g_N and μ_N depend on the nucleus under study.)

Maxwell-Boltzmann distribution

In practice, EPR samples consist of collections of many paramagnetic species, and not single isolated paramagnetic centers. If the population of radicals is in thermodynamic equilibrium, its statistical distribution is described by the Maxwell-Boltzmann equation

$$\frac{n_{\text{upper}}}{n_{\text{lower}}} = \exp\left(-\frac{E_{\text{upper}} - E_{\text{lower}}}{kT}\right) = \exp\left(-\frac{\Delta E}{kT}\right) = \exp\left(-\frac{\epsilon}{kT}\right) = \exp\left(-\frac{h\nu}{kT}\right)$$

where n_{upper} is the number of paramagnetic centers occupying the upper energy state, k is the Boltzmann constant, and T is the temperature in kelvins. At 298 K, X-band microwave frequencies ($\nu \approx 9.75$ GHz) give $n_{\text{upper}}/n_{\text{lower}} \approx 0.998$, meaning that the upper energy level has a smaller population than the lower one. Therefore, transitions from the lower to the higher level are more probable than the reverse, which is why there is a net absorption of energy.

The sensitivity of the EPR method (i.e., the minimum number of detectable spins N_{min}) depends on the photon frequency ν according to

$$N_{\text{min}} = \frac{k_1 V}{Q_0 k_f \nu^2 P^{1/2}}$$

where k_1 is a constant, V is the sample's volume, Q_0 is the unloaded quality factor of the microwave cavity (sample chamber), k_f is the cavity filling coefficient, and P is the microwave power in the spectrometer cavity. With k_f and P being constants, $N_{\text{min}} \sim (Q_0 \nu^2)^{-1}$, i.e., $N_{\text{min}} \sim \nu^{-\alpha}$, where $\alpha \approx 1.5$. In practice, α can change varying from 0.5 to 4.5 depending on spectrometer characteristics, resonance conditions, and sample size. In other words, the higher the spectrometer frequency the lower the detection limit (N_{min}), meaning greater sensitivity.

Spectral parameters

In real systems, electrons are normally not solitary, but are associated with one or more atoms. There are several important consequences of this:

1. An unpaired electron can gain or lose angular momentum, which can change the value of its g -factor, causing it to differ from g_e . This is especially significant for chemical systems with transition-metal ions.
2. If an atom with which an unpaired electron is associated has a non-zero nuclear spin, then its magnetic moment will affect the electron. This leads to the phenomenon of hyperfine coupling, analogous to J-coupling in NMR, splitting the EPR resonance signal into doublets, triplets and so forth.
3. Interactions of an unpaired electron with its environment influence the shape of an EPR spectral line. Line shapes can yield information about, for example, rates of chemical reactions.
4. The g -factor and hyperfine coupling in an atom or molecule may not be the same for all orientations of an unpaired electron in an external magnetic field. This anisotropy depends upon the electronic structure of the atom or molecule (e.g., free radical) in question, and so can provide information about the atomic or molecular orbital containing the unpaired electron.

The g factor

Knowledge of the g -factor can give information about a paramagnetic center's electronic structure. An unpaired electron responds not only to a spectrometer's applied magnetic field B_0 , but also to any local magnetic fields of atoms or molecules. The effective field B_{eff} experienced by an electron is thus written

$$B_{\text{eff}} = B_0(1 - \sigma)$$

where σ includes the effects of local fields (σ can be positive or negative). Therefore, the $h\nu = g\mu_B B_{\text{eff}}$ resonance condition (above) is rewritten as follows:

$$h\nu = g\mu_B B_{\text{eff}} = g\mu_B B_0(1 - \sigma)$$

The quantity $g_e(1 - \sigma)$ is denoted g and called simply the g -factor, so that the final resonance equation becomes

$$h\nu = g\mu_B B_0$$

This last equation is used to determine g in an EPR experiment by measuring the field and the frequency at which resonance occurs. If g does not equal g_e the implication is that the ratio of the unpaired electron's spin magnetic moment to its angular momentum differs from the free electron value. Since an electron's spin magnetic moment is constant (approximately the Bohr magneton), then the electron must have gained or lost angular momentum through spin-orbit coupling. Because the mechanisms of spin-orbit coupling are well understood, the magnitude of the change gives information about the nature of the atomic or molecular orbital containing the unpaired electron.

Hyperfine coupling

Since the source of an EPR spectrum is a change in an electron's spin state, it might be thought that all EPR spectra would consist of a single line. However, the interaction of an unpaired electron, by way of its magnetic moment, with nearby nuclear spins, results in additional allowed energy states and, in turn, multi-lined spectra. In such cases, the spacing between the EPR spectral lines indicates the degree of interaction between the unpaired electron and the perturbing nuclei. The hyperfine coupling constant of a nucleus is directly related to the spectral line spacing and, in the simplest cases, is essentially the spacing itself.

Two common mechanisms by which electrons and nuclei interact are the Fermi contact interaction and by dipolar interaction. The former applies largely to the case of isotropic interactions (independent of sample orientation in a magnetic field) and the latter to the case of anisotropic interactions (spectra dependent on sample orientation in a magnetic field). Spin polarization is a third mechanism for interactions between an unpaired electron and a nuclear spin, being especially important for π -electron organic radicals, such as the benzene radical anion. The symbols " a " or " A " are used for isotropic hyperfine coupling constants while " B " is usually employed for anisotropic hyperfine coupling constants.^[2]

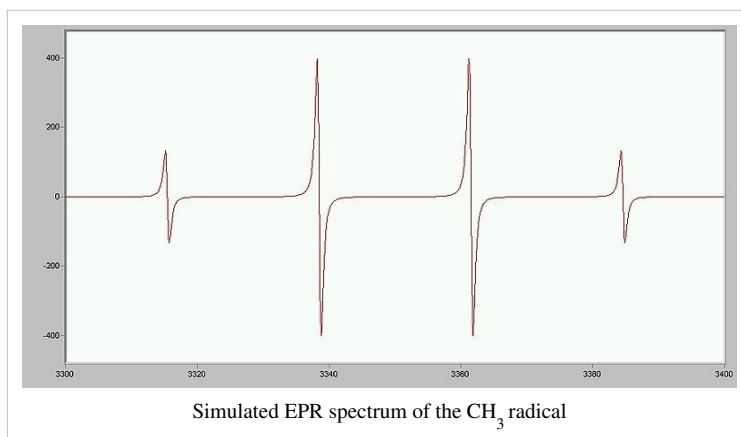
In many cases, the isotropic hyperfine splitting pattern for a radical freely tumbling in a solution (isotropic system) can be predicted.

- For a radical having M equivalent nuclei, each with a spin of I , the number of EPR lines expected is $2MI + 1$. As an example, the methyl radical, CH_3 , has three ^1H nuclei each with $I = 1/2$, and so the number of lines expected is $2MI + 1 = 2(3)(1/2) + 1 = 4$, which is as observed.
- For a radical having M_1 equivalent nuclei, each with a spin of I_1 , and a group of M_2 equivalent nuclei, each with a spin of I_2 , the number of lines expected is $(2M_1I_1 + 1)(2M_2I_2 + 1)$. As an example, the methoxymethyl radical, $\text{H}_2\text{C}(\text{OCH}_3)$, has two equivalent ^1H nuclei each with $I = 1/2$ and three equivalent ^1H nuclei each with $I = 1/2$, and so the number of lines expected is $(2M_1I_1 + 1)(2M_2I_2 + 1) = [2(2)(1/2) + 1][2(3)(1/2) + 1] = [3][4] = 12$, again as observed.

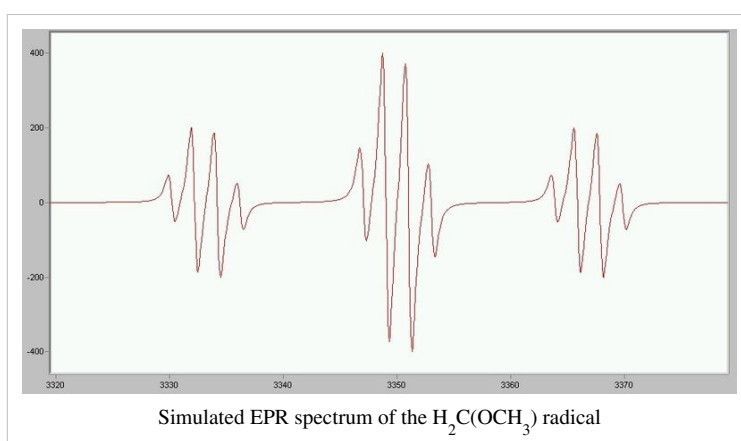
- The above can be extended to predict the number of lines for any number of nuclei.

While it is easy to predict the number of lines a radical's EPR spectrum should show, the reverse problem, unraveling a complex multi-line EPR spectrum and assigning the various spacings to specific nuclei, is more difficult.

In the oft-encountered case of $I = 1/2$ nuclei (e.g., ^1H , ^{19}F , ^{31}P), the line intensities produced by a population of radicals, each possessing M equivalent nuclei, will follow Pascal's triangle. For example, the spectrum at the right shows that the three ^1H nuclei of the CH_3 radical give rise to $2MI + 1 = 2(3)(1/2) + 1 = 4$ lines with a 1:3:3:1 ratio. The line spacing gives a hyperfine coupling constant of $a_{\text{H}} = 23 \text{ G}$ for each of the three ^1H nuclei. Note again that the lines in this spectrum are *first derivatives* of absorptions.



As a second example, consider the methoxymethyl radical, $\text{H}_2\text{C}(\text{OCH}_3)$. The two equivalent methyl hydrogens will give an overall 1:2:1 EPR pattern, each component of which is further split by the three methoxy hydrogens into a 1:3:3:1 pattern to give a total of $3 \times 4 = 12$ lines, a triplet of quartets. A simulation of the observed EPR spectrum is shown at the right, and agrees with the 12-line prediction and the expected line intensities. Note that the smaller coupling constant (smaller line spacing) is due to the three methoxy hydrogens, while the larger coupling constant (line spacing) is from the two hydrogens bonded directly to the carbon atom bearing the unpaired electron. It is often the case that coupling constants decrease in size with distance from a radical's unpaired electron, but there are some notable exceptions, such as the ethyl radical (CH_2CH_3).



Resonance linewidth definition

Resonance linewidths are defined in terms of the magnetic induction B , and its corresponding units, and are measured along the x axis of an EPR spectrum, from a line's center to a chosen reference point of the line. These defined widths are called halfwidths and possess some advantages: for asymmetric lines values of left and right halfwidth can be given. The halfwidth ΔB_h is the distance measured from the line's center to the point in which absorption value has half of maximal absorption value in the center of resonance line. First inclination width $\Delta B_{1/2}$ is a distance from center of the line to the point of maximal absorption curve inclination. In practice, a full definition of linewidth is used. For symmetric lines, halfwidth $\Delta B_{1/2} = 2\Delta B_h$, and full inclination width $\Delta B_{max} = 2\Delta B_{1s}$.

Applications

EPR spectroscopy is used in various branches of science, such as chemistry and physics, for the detection and identification of free radicals and paramagnetic centers such as F centers. EPR is a sensitive, specific method for studying both radicals formed in chemical reactions and the reactions themselves. For example, when frozen water (solid H_2O) is decomposed by exposure to high-energy radiation, radicals such as H, OH, and HO_2 are produced. Such radicals can be identified and studied by EPR. Organic and inorganic radicals can be detected in electrochemical systems and in materials exposed to UV light. In many cases, the reactions to make the radicals and the subsequent reactions of the radicals are of interest, while in other cases EPR is used to provide information on a radical's geometry and the orbital of the unpaired electron.

Medical and biological applications of EPR also exist. Although radicals are very reactive, and so do not normally occur in high concentrations in biology, special reagents have been developed to spin-label molecules of interest. These reagents are particularly useful in biological systems. Specially-designed nonreactive radical molecules can attach to specific sites in a biological cell, and EPR spectra can then give information on the environment of these so-called spin-label or spin-probes.

A type of dosimetry system has been designed for reference standards and routine use in medicine, based on EPR signals of radicals from irradiated polycrystalline α -alanine (the alanine deamination radical, the hydrogen abstraction radical, and the $(\text{CO}^-(\text{OH}))=\text{C}(\text{CH}_3)\text{NH}_2^+$ radical). This method is suitable for measuring gamma and x-rays, electrons, protons, and high-linear energy transfer (LET) radiation of doses in the 1 Gy to 100 kGy range.^[3]

EPR spectroscopy can only be applied to systems in which the balance between radical decay and radical formation keeps the free-radicals concentration above the detection limit of the spectrometer used. This can be a particularly severe problem in studying reactions in liquids. An alternative approach is to slow down reactions by studying samples held at cryogenic temperatures, such as 77 K (liquid nitrogen) or 4.2 K (liquid helium). An example of this work is the study of radical reactions in single crystals of amino acids exposed to x-rays, work that sometimes leads to activation energies and rate constants for radical reactions.

The study of radiation-induced free radicals in biological substances (for cancer research) poses the additional problem that tissue contains water, and water (due to its electric dipole moment) has a strong absorption band in the microwave region used in EPR spectrometers.

EPR also has been used by archaeologists for the dating of teeth. Radiation damage over long periods of time creates free radicals in tooth enamel, which can then be examined by EPR and, after proper calibration, dated. Alternatively, material extracted from the teeth of people during dental procedures can be used to quantify their cumulative exposure to ionizing radiation. People exposed to radiation from the Chernobyl disaster have been examined by this method.^{[4] [5]}

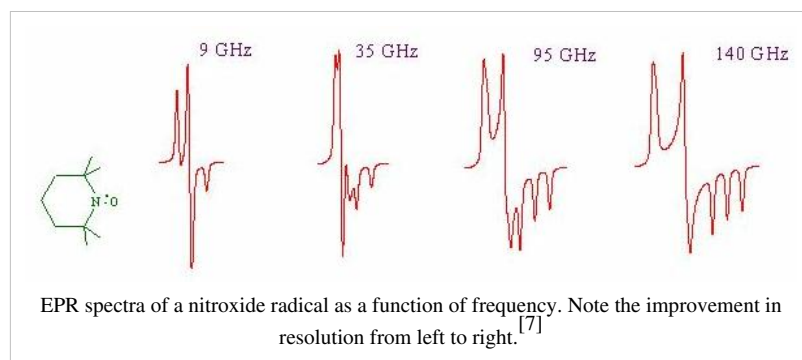
Radiation-sterilized foods have been examined with EPR spectroscopy, the aim being to develop methods to determine if a particular food sample has been irradiated and to what dose.

Because of its high sensitivity, EPR was used recently to measure the quantity of energy used locally during a mechanochemical milling process.^[6]

High-field high-frequency measurements

High-field-high-frequency EPR measurements are sometimes needed to detect subtle spectroscopic details. However, for many years the use of electromagnets to produce the needed fields above 1.5 T was impossible, due principally to limitations of traditional magnet materials. The first multifunctional millimeter EPR spectrometer with a superconducting solenoid was described in the early 1970s by Prof. Y. S. Lebedev's group (Russian Institute of Chemical Physics, Moscow) in collaboration with L. G. Oranski's group (Ukrainian Physics and Technics Institute, Donetsk) which began working in the Institute of Problems of Chemical Physics, Chernogolovka around 1975.^[7] Two decades later, a W-band EPR spectrometer was produced as a small commercial line by the German Bruker

Company, initiating the expansion of W-band EPR techniques into medium-sized academic laboratories. Today there still are only a few scientific centers in the world capable of high-field-high-frequency EPR, among them are the Grenoble High Magnetic Field Laboratory in Grenoble, France, the Physics Department in Freie Universität Berlin, the National High Magnetic Field Laboratory in Tallahassee, US, the National Center for Advanced ESR Technology (ACERT) at Cornell University in Ithaca, US, the Department of Physiology and Biophysics at Albert Einstein College of Medicine, Bronx, NY, the IFW in Dresden, Germany, the Institute of Physics of Complex Matter in Lausanne in Switzerland, and the Institute of Physics of the Leiden University, Netherlands.



Waveband	L	S	C	X	P	K	Q	U	V	E	W	F	D	—	J	—
λ/mm	300	100	75	30	20	12.5	8.5	6	4.6	4	3.2	2.7	2.1	1.6	1.1	0.83
ν/GHz	1	3	4	10	15	24	35	50	65	75	95	111	140	190	285	360
B_0/T	0.03	0.11	0.14	0.33	0.54	0.86	1.25	1.8	2.3	2.7	3.5	3.9	4.9	6.8	10.2	12.8

The EPR waveband is stipulated by the frequency or wavelength of a spectrometer's microwave source (see Table).

EPR experiments often are conducted at X and, less commonly, Q bands, mainly due to the ready availability of the necessary microwave components (which originally were developed for radar applications). A second reason for widespread X and Q band measurements is that electromagnets can reliably generate fields up to about 1 tesla. However, the low spectral resolution over g -factor at these wavebands limits the study of paramagnetic centers with comparatively low anisotropic magnetic parameters. Measurements at $\nu > 40$ GHz, in the millimeter wavelength region, offer the following advantages:

1. EPR spectra are simplified due to the reduction of second-order effects at high fields.
2. Increase in orientation selectivity and sensitivity in the investigation of disordered systems.
3. The informativity and precision of pulse methods, e.g., ENDOR also increase at high magnetic fields.
4. Accessibility of spin systems with larger zero-field splitting due to the larger microwave quantum energy $h\nu$.
5. The higher spectral resolution over g -factor, which increases with irradiation frequency ν and external magnetic field B_0 . This is used to investigate the structure, polarity, and dynamics of radical microenvironments in spin-modified organic and biological systems through the spin label and probe method. The figure shows how spectral resolution improves with increasing frequency.
6. Saturation of paramagnetic centers occurs at a comparatively low microwave polarizing field B_1 , due to the exponential dependence of the number of excited spins on the radiation frequency ν . This effect can be successfully used to study the relaxation and dynamics of paramagnetic centers as well as of superslow motion in the systems under study.
7. The cross-relaxation of paramagnetic centers decreases dramatically at high magnetic fields, making it easier to obtain more-precise and more-complete information about the system under study.^[7]

See also

- Ferromagnetic resonance
- Spin labels
- Site-directed spin labeling
- Spin trapping

Further reading

Many good books and papers are available on the subject of EPR spectroscopy, including those listed here. Essentially all details in this article can be found in these.

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External links

- NMRWiki.ORG ^[5] project
- Electron Magnetic Resonance Program ^[8] National High Magnetic Field Laboratory

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